November 15, 2005

Mr. Michael Gallagher
PBT Coordinator
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FAX: 360-407-6884

RE: Inclusion of Decabromodiphenyl Ether in the Department of Ecology's Proposed Rule regarding Persistent Bioaccumulative Toxins (PBTs) (Chapter 173-333 WAC).

Dear Mr. Gallagher:

The Bromine Science and Environmental Forum (BSEF) is a global industry association comprised of the major manufacturers of brominated flame retardants and our mission is to further the scientific understanding of our products. As such, BSEF and its member companies have sponsored numerous studies on the potential health and environmental effects of our products, and we have engaged the services of individuals with in-depth knowledge of the toxicology of our products.

BSEF has two major concerns with the inclusion of decabromodiphenyl ether (Deca-BDE) in the Proposed Rule regarding Persistent Bioaccumulative Toxins (PBTs) (Chapter 173-333 WAC), some of which have been expressed to the Department of Ecology previously:

1. Decabromodiphenyl ether (Deca-BDE) is not toxic or bioaccumulative. Further, Deca-BDE does not meet the Department of Ecology's criteria for classification as a persistent, bioaccumulative and toxic substance and therefore should not be included in this proposed rule.
2. The Department of Ecology appears to have adopted as fact the contention that Deca-BDE degrades into lower congeners that are of concern from human health or environmental perspectives, and to have done so absent clear or even significant scientific evidence of such degradation.

Additionally, the State of Wisconsin has not classified Deca-BDE as a PBT. In its "Summary Technical Background Information for the Proposed PBT List," the Department of Ecology incorrectly states on page 59 that, "PBDEs have been identified as PBTs by the State of Wisconsin (WDNR, 2005)." According to Wisconsin Department of Natural Resources staff, Wisconsin does not have in place an administrative rule that lists Deca-BDE as a PBT, and there is no regulation of Deca-BDE in Wisconsin as a PBT.

On July 29, 2005, BSEF filed detailed comments with the Department of Ecology on why Deca-BDE does not meet the Department criteria for classification as a PBT. We ask that those comments be incorporated as part of this record, and also submit the following additional comments.

Issue 1: Decabromodiphenyl ether (Deca-BDE) does not meet the Department of Ecology's criteria for classification as a persistent, bioaccumulative toxin.

The Department of Ecology proposes that a substance would be considered persistent, bioaccumulative and toxic if:

- It's half-life in water, soil or sediment is > 60 days;
- It's bioconcentration/bioaccumulation factor is > 1000; and
- It is a known carcinogen, reproductive or neurologic toxicant, has a reference dose (RfD) of < 0.003 mg/kg/d, or is toxic to fish on chronic exposure.

(Detailed comments on the proposed criteria themselves are enclosed in Attachment A.)

Specifically, while Deca-BDE meets the Department's proposed criteria for persistence, it does not meet the proposed criteria for a bioaccumulative and toxic substance, and cannot therefore be properly classified as a PBT.

Persistence. Deca-BDE would be considered persistent under the Department's proposed criteria. Its estimated (EPIwin, v3.04) half-lives in water, soil and sediment are all > 60 days.

Bioconcentration/Bioaccumulation. Deca-BDE does not meet the Department's proposed criteria for this end point. Deca-BDE's measured fish BCF is <50.

Toxic. Deca-BDE does not meet the proposed criteria for this end point. Deca-BDE is not a known carcinogen, reproductive, developmental or neurological toxicant. Deca-BDE's oral RfD, established by the U.S. National Academy of Sciences (2000) is 4 mg/kg/d. Deca-BDE is not toxic to fish, daphnia or algae, either acutely or chronically, at its limit of saturation in water. Deca-BDE is not toxic to sediment organisms, bacteria, or terrestrial plants.

Data supporting these statements are included in the enclosed Attachment B: IUCLID file on Deca-BDE.

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Issue 2: The Department of Ecology appears to have adopted as fact the contention that Deca-BDE degrades into lower congeners that are of concern from human health or environmental perspectives, and to have done so absent clear or even significant scientific evidence of such degradation.

The proposed rule appears to include Deca-BDE as a PBT on the basis that it degrades into lower congeners that may themselves meet the PBT profile. In fact, there is no evidence that, in the environment, Deca-BDE degrades or debrominates in any significant manner into lower-brominated PBDE congeners of concern. The pattern of congeners detected in the environment is characteristic of the congeners present in the commercial Penta-BDE product, which is no longer manufactured or used. Further, the Department of Ecology has not identified which lower brominated congeners in believes Deca-BDE degrades to and why those congeners meet the proposed PBT criteria.

The Department of Ecology appears to base its position regarding degradation largely on laboratory studies. These studies must be carefully evaluated in order to determine if their results have relevance to the actual environment. In our opinion, the majority of these studies do not have relevance in the real environment. For example, photolyis studies performed in organic solvents are not representative of actual environmental conditions. Also, anaerobic sewage sludge studies conducted for more than 200 days are not representative of the typical 28-day sludge retention times.

The EU Risk Assessment (Deca-BDE update August 2005) evaluated all published data on Deca-BDE degradation available as of August 2005 and concluded on page 48:

"Importantly, results of a number of sediment core monitoring studies were reported in the previous risk assessment reports, and these did not provide any evidence of debromination (in either freshwater or marine environments). In addition, the degradation studies reported above appear to result in a wide distribution of congeners. This pattern is not reflected in environmental samples, which are always dominated by the congeners present in the various commercial products. Nevertheless, the pattern could be masked for this very reason. In summary, the available monitoring data provide little evidence for debromination being a significant degradation mechanism for decabromodiphenyl ether in the environment (and hence a major source of lower brominated congeners).

Consequently the new data serve to reinforce the existing concerns, but do not lead the rapporteur to conclude that there is actually a risk. The conclusions of the previous assessment therefore remain essentially the same, but additional investigations are necessary. The rapporteur recognises that there are uncertainties in drawing this conclusion."

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This conclusion was endorsed by **all the technical experts** from the EU member states in the EU Technical Committee on New and Emerging Substances discussions.

Additionally, numerous laboratory investigations have demonstrated that when Deca-BDE undergoes reductive debromination to lower BDEs, it does so in a virtually non-specific manner (Keum and Li, 2005). Research has demonstrated that selective formation of BDEs-47, 99, 100, 153, 154 – the lower-brominated BDEs of concern and those most commonly found in biota – does not occur by the reductive debromination of Deca-BDE.

BSEF also offers the following comments on specific issues:

1. Photolysis

Various publications have demonstrated that Deca-BDE can be reduced photolytically to lower BDEs and that the rate of photolysis decreases with decreasing degrees of bromination. Moreover, the described photolysis reactions typically produce a wide range of congeners, which does not resemble the congener pattern found in the environment. This is also confirmed by environmental monitoring studies (see below).

With respect to Eriksson's work (Eriksson et al 2004):

- No evidence was found for formation of environmentally relevant PBDE congeners (e.g., BDE 47, 99, 100, 153);
- Eriksson specifically states that photolysis in pure water was rather poor and…"no degradation products were found."

As mentioned above, it is extremely important to consider whether or not the described processes are likely to occur in the real environment. For example, irradiation of soil and/or sediment spiked with Deca-BDE has been shown to result in Deca-BDE degradation and the formation of lower BDEs. In contrast, irradiation of a field sample of real soil that had been amended several years prior with Deca-BDE-containing sewage sludge resulted in no Deca-BDE degradation. These results, presented by Cynthia de Wit at Dioxin 2005, demonstrate the dramatic difference in the behavior of laboratory samples and actual field samples.

The EU Risk Assessment also evaluated the Eriksson study and came to the following conclusion:

"Although these new data provide additional evidence that decabromodiphenyl ether could photodegrade to form more toxic and accumulative products in the presence of water, it is not possible to extrapolate these results directly to the environment for a

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number of reasons (as outlined by Bezares-Cruz et al. (2004)). These include absorption of decabromodiphenyl ether onto colloidal particles in the environment, the attenuation of light by humic materials (and other materials) in the environment and the generally lower concentrations and/or less favourable hydrogen donors present in natural waters compared with the conditions used in the laboratory studies. Similar conclusions were drawn in the previous risk assessment report:

Overall, although it can be concluded that formation of lower brominated diphenyl ethers and brominated dibenzofurans can occur from the photolysis of decabromodiphenyl ether in the environment, the actual significance of the process is likely to be limited owing to the lack of exposure to light of the bulk of decabromodiphenyl ether in the environment. It is considered unlikely that such photolysis reactions of decabromodiphenyl ether could explain the current widespread occurrence of tetra-, penta- and hexabromodiphenyl ether congeners in the environment. Instead, it is much more likely that this is mainly the result of the emissions of the commercial penta- and octabromodiphenyl ether flame retardants. However any photolysis of decabromodiphenyl ether that does occur in the environment could make a (probably small) contribution to the levels of the lower brominated diphenyl ether congeners and also possibly brominated dibenzofurans present in the environment."

This conclusion would therefore still seem to be appropriate based on the new photolysis data."

2. Anaerobic degradation reactions

Deca-BDE is found in the environment mainly in sediment, so Deca-BDE's fate in that matrix is important when considering Deca-BDE's overall fate in the environment. The most relevant test for that scenario, a simulation degradation study with anaerobic sediments using 14C-labelled Deca-BDE, did not find any indications for degradation of Deca-BDE over a 32-week period. Likewise, DeWit reported no evidence of degradation in anaerobic sediment after two years incubation.

Gerecke et al. (2005) recently reported on a 238 day study of Deca-BDE's potential to undergo anaerobic degradation in a sludge digester system. No evidence of degradation was observed at 114 days. Even after an incubation of 238 days, 8.5 times the typical residence time in an anaerobic digester, only a slight increase in the concentration of two Nona-BDE's, which are typically minor impurities in the commercial Deca-BDE product, was observed. Furthermore, the study reported that the Nona-BDE's detected were lacking a bromine atom in the para-position of the molecule. The predominant PBDE congeners detected in the environment, however, are brominated in that

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position. The study strongly suggests, therefore, that this mechanism is not responsible for the PBDE congeners found in the environment.

Gerecke works are also cited as evidence for Deca-BDE degradation during sunlight exposure. Gerecke conducted no photochemical experiments.

3. Methoxy derivatives

Methoxylated PBDE derivatives are known to be naturally occurring compounds. The general consensus of the scientific community is that methoxy-PBDEs detected in the environment are predominantly of natural origin. Research supporting this position can be found in the article *Two Abundant Bioaccumulated Halogenated Compounds Are Natural Products*, by Emma L. Teuten, Li Xu and Christopher M. Reddy. (SCIENCE 307 (2005) 917-919). This position is also supported by the work of Walter Vetter et al.

4. Environmental monitoring data

Laboratory results can provide valuable information about potential chemical reactions and allow researchers to study reaction pathways, etc. It is, however, important to consider the rate at which these reactions occur in the environment versus the rate at which they occur in the laboratory. Environmental monitoring study findings provide solid information for comparison and contrast.

Monitoring studies indicate that Deca-BDE is not the source of BDE 47, 99 and 100, but that these congeners were associated with the Penta-BDE product. Monitoring data from European sediments laid down over 20 years do not support degradation of Deca-BDE (de Boer 2001). In this work, based on sediment cores, de Boer et al. concluded that significant amounts of lesser brominated diphenyl ethers were unlikely to be formed from Deca-BDE. Although the sediment concentration of Deca-BDE increased in more recent years, no parallel increase in the concentrations of lesser brominated diphenyl ethers (e.g. tetra- to penta- congeners) occurred, and there was no indication of increasing levels of nona- and octabromodiphenyl ethers.

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Other European studies show similar results. Similar results have also been found in North America. Rayne and Ikonomou investigated PBDEs in sediments in the Fraiser River in British Columbia, Canada.[1] Their analysis of the congener pattern found in the environment indicates that the congeners present originated from the commercial Penta-BDE and Octa-BDE products, and that Deca-BDE was not the source.

[1] Ikonomou M. G., Rayne S. and Addison R. F. (2002). Exponential increases of brominated flame retardants, polybrominated diphenyl ethers, in the Canadian Arctic from 1981 to 2000. Environ. Sci. Technol., **36**, 1886-1892.

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Note: We propose to quote Martin van den Berg from his paper, re. no evidence that degradation of deca is responsible for the components of penta found in the environment, but so far requests for this document have not borne fruit.

Conclusion

Section 173-333 WAC states that the purpose of the chapter is to establish the criteria that the Department of Ecology will use to identify persistent bioaccumulative toxins that pose human health or environmental threats in the State of Washington. The rule creates objective, measurable values in Section 173-333-320 for persistence, bioaccumulation and toxicity, consistent with what BSEF believes is the intent of the rule: To create a clear standard for designating chemicals as PBTs so that the state can focus its resources on areas of true scientific concern.

Subsection 3 of 173-333-320 (degradation) is inconsistent with this purpose because there is no criteria established for objectively determining what constitutes a level of degradation that should be considered cause for concern. Just as all substances can have toxic effects at a high enough concentration, all substances (save elements) will degrade – to some extent and under some circumstances – into other chemical configurations. If degradation is to be considered, the Department of Ecology should establish clear criteria for identifying and evaluating degradation, including the level of scientific evidence required to show degradation. The Department of Ecology should not be using a proposed rule to arbitrarily add chemicals to the PBT list and thereby circumvent the criteria set forth in Subsection (2), paragraphs a, b, and c of the same section.

BSEF has stated repeatedly, and supported its position with scientific evidence, that Deca-BDE does not meet the criteria set forth in the proposed rule for listing as a PBT. The European Union completed a comprehensive, 10-year risk assessment on Deca-BDE, evaluating more than 580 independent scientific studies, and concluded that Deca-BDE does not pose a threat to human health or the environment.

It is therefore difficult to understand how the Department of Ecology has arrived at a conclusion that is exactly opposite that of the European Union without having performed an in-depth analysis of the available literature, much less an analysis even remotely approaching that undertaken by the EU. Further, it is difficult to understand why the EU risk assessment – the most comprehensive analysis ever performed on any single flame retardant in history – as well as the conclusions and subsequent regulatory decisions based on that analysis, appear not to have been included in the Department of Ecology's deliberations on the PBT rule in any meaningful manner whatsoever, despite having been brought to the Department's attention.

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BSEF representatives have participated in the PBT rulemaking in good faith and have tried to bring both sound science and real world chemical experience to the process. We are, however, gravely concerned at this time that the final rule, with regard to Deca-BDE, will likely contain a policy position that is scientifically insupportable, contrary to the very criteria of the rule itself and damaging to legitimate and significant business interests. As such, the entire rulemaking process and final rule will be open to question.

We are also providing the Department of Ecology an array of scientific papers supporting the arguments that we have made throughout the course of this rulemaking. Attached to these comments is Attachment A, a strike through of the actual proposed rule, Attachment B, a set of reference documents mentioned in the body of the comments, and Attachment C, a Table of Contents for a comprehensive set of documents in CD format, which will be hand-delivered under separate cover.

We respectfully and sincerely urge the Department of Ecology to review this material and to reconsider its wholly inappropriate inclusion of Deca-BDE in the PBT rule. On July 29, 2005, BSEF filed detailed comments with the Department of Ecology on why Deca-BDE does not meet the Department criteria for classification as a PBT. We ask that those comments be incorporated as part of this record, and also submit the following additional comments.

Sincerely,

Raymond B. Dawson, PhD.
Chairman
BSEF

David C. Sanders, PhD.
Director, North America
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Chapter 173-333 WAC

PERSISTENT BIOACCUMULATIVE TOXINS

PART I
GENERAL PROVISIONS

NEW SECTION

WAC 173-333-100 Introduction. Persistent, bioaccumulative and toxic substances ~~toxins~~ (PBTs) are chemicals that may pose a unique threat to human health and the environment in Washington state. They remain in the environment for long periods of time, are hazardous to the health of humans and wildlife, and can build up in the food chain~~., and can be transported long distances and readily move between air, land and water media.~~[The definition of PBT – including the definition set forth by the U.S. Environmental Protection Agency – does not typically include the long range transport or ready movement between media and the criteria set for PBT substances in this document do not include that for long range transport or movement between media. The generally accepted definition of PBT only includes toxicity to and bioaccumulation in aquatic organisms. We suggest the Department of Ecology reconsider the proposed criteria.]

Because of the unique threat that these PBTs pose, special attention is necessary to identify actions that will reduce and eliminate threats to human health and the environment. While ecology addresses PBTs through existing regulatory and nonregulatory programs, there remains a need for multimedia, cross-program measures that will reduce and phase-out releases and uses of PBTs over time.

The goal of this chapter is to reduce and phase-out PBT uses, releases and exposures in Washington. Ecology recognizes that many factors will influence whether and when this goal can be attained and that those factors will often vary depending on the PBT and the uses of the PBT. These factors include environmental and human health benefits, economic and social costs, technical feasibility, availability of safer substitutes, and consistency with other regulatory requirements. This chapter establishes a process that ecology will use to evaluate and identify actions that should be taken for particular PBTs. This process is designed to enhance actions being taken under other environmental laws and regulations.

NEW SECTION

WAC 173-333-110 What is the purpose of this chapter? The purpose of this chapter is to:

(1) Establish criteria ecology will use to identify persistent bioaccumulative ~~toxins~~ toxicants [NOTE: the term 'toxins' is defined as substances which cause adverse effects and which are produced by biological systems; e.g. venoms, algal secondary metabolites, bacterial or fungal toxins such as botulinum or aflatoxin, etc.] that pose human health or environmental threats in Washington state;

(2) Establish a list of persistent bioaccumulative and toxic substances~~toxins~~;

(3) Establish procedures ecology will use to review and periodically update the list;

(4) Establish criteria for selecting persistent bioaccumulative and toxic substances ~~toxins~~ for which ecology will prepare chemical action plans;

(5) Define the scope and content of chemical action plans and establish the process ecology will use to prepare those plans; and

(6) Define the processes ecology will use to coordinate the implementation of this chapter with the department of health and other agencies.

NEW SECTION

WAC 173-333-120 Applicability. (1) This chapter applies to the department of ecology (ecology). This chapter does not impose new requirements on persons using or releasing PBTs, and it does not create new authorities nor does it constrain existing authorities for ecology.

(2) This chapter provides for public involvement opportunities to allow interested persons to participate in the ecology processes for identifying PBTs and developing recommendations on measures to address uses and releases of PBTs.

NEW SECTION

WAC 173-333-130 Exemptions to the PBT list. Any pesticide with a currently valid registration that has been issued by the Environmental Protection Agency under the Federal Insecticide, Fungicide and Rodenticide Act, 7 U.S.C. 136 et seq., or any fertilizer regulated under the Washington Fertilizer Act, chapter 15.54 RCW, will not be included on the ~~persistent bioaccumulative toxin~~ PBT list established under this chapter.

If the Department intends to exempt substances that are currently regulated under other statutes, then consideration should be given to extending this exemption to industrial chemicals that are regulated under the U.S. Toxic Substances Control Act (TSCA). The Department of Ecology should explain its concerns with TSCA and why it believes additional measures must be taken at the state level.

NEW SECTION

WAC 173-333-140 Administrative principles. (1) **Scientific information.** Ecology will base decisions on PBTs on sound public policy and credible scientific information. However, ecology believes that lack of full scientific consensus should not be used as a justification for delaying reasonable measures to prevent harm to human health or the environment.

(2) **Public involvement.** Ecology will provide opportunities for public involvement during the decision-making processes for identifying PBTs and preparing a CAP.

(3) **Clear documentation.** Ecology will provide clear and understandable descriptions and rationale for decisions implementing this chapter.

(4) **Predictability.** Ecology will implement this chapter in ways that allow stakeholders, interest groups, and the public to plan their participation in decision-making processes and future responses to recommendations that result from those processes.

(5) **Coordination.** Ecology will coordinate with federal and state agencies, local governments, tribes, and other interested parties in the development and implementation of CAPs and when revising the PBT list.

(6) **Rule amendments.** When amending any portion of this rule, Ecology will follow the requirements of the Administrative Procedure Act (APA), chapter 34.05 RCW.

PART II
DEFINITIONS

NEW SECTION

The following definitions apply under this rule.

WAC 173-333-200 Definitions. "Administrative Procedure Act" or **"APA"** means the Washington Administrative Procedure Act, chapter 34.05 RCW.

"Bioaccumulation" means the process by which substances, with repeated exposure, increase in concentration in living organisms as they take in contaminated air, water, soil, sediment or food because the substances are very slowly metabolized or excreted.

"Bioaccumulation factor" or **"BAF"** means the ratio of the concentration of a chemical in an organism to the concentration of the chemical in the surrounding environment. The BAF represents

exposures/uptake via all routes, e.g. in the case of fish - food as well as water. ~~The BAF is a measure of the extent to which the organism accumulates the chemical as a result of uptake through ingestion as well as contact from contaminated media, such as water.~~

"Bioconcentration factor" or **"BCF"** means the ratio of the concentration of a chemical in fish tissue ~~an organism~~ to the concentration of the chemical in water ~~in the surrounding environment.~~ The BCF represents exposures via water through the gills.~~is a measure of the extent of chemical partitioning between an organism and the surrounding environment.~~

"Carcinogen" means a chemical or chemical group that is known or suspected to cause ~~increase the probability of developing~~ cancer. For purposes of implementing this chapter, the term carcinogen applies to substances that have been identified as "carcinogenic to humans" or "likely to be carcinogenic to humans" by the U.S. Environmental Protection Agency, as a Group 1, 2A or 2B carcinogen by the International Agency for Research on Cancer or as a "known to be a human carcinogen" or "reasonably anticipated to be a human carcinogen" by the National Toxicology Program.

"Chemical" means a naturally occurring element, mixture, or group of organic and inorganic compounds that is produced by or used in a chemical process.

"Chemical action plan" or **"CAP"** means a plan that identifies, characterizes and evaluates uses and releases of a specific PBT or a group of PBTs and recommends actions to protect human health or the environment.

"Chemical group" means a grouping of chemicals which share a common chemical structure and common toxicological properties/modes of action. [NOTE: On what basis will the Department determine that certain chemicals can be classified as a group? This approach may be valid as a screening tool for chemicals with insufficient data (e.g. as used by EPA's New Chemicals Program), but chemicals with existing data should not be grouped.]

"Credible scientific information" means information that is based on a theory or technique that is generally acceptable in the relevant scientific community or has been collected or derived using standard or generally accepted methods and protocols and appropriate quality assurance and control procedures.

"Cross-media transfer of chemicals" means the movement of a chemical from one medium, such as air, water, soil, or sediment, to another. [Any chemical will do this to some extent. We would recommend a more specific definition.]

"Degradation" means the processes by which organic chemicals are transformed into derivative chemicals and ultimately broken down to ???? [additional criteria required to complete definition].

"Developmental or reproductive toxicant" means a chemical or chemical group that is known or suspected to cause adverse effects on development or reproduction. For purposes of implementing this chapter, the term developmental or reproductive toxicant applies to

chemicals or chemical groups identified as posing developmental or reproductive hazards by the National Toxicology Program or chemicals or chemical groups with sufficient evidence of a developmental or reproductive hazard in humans or experimental animals consistent with the United States Environmental Protection Agency's Guidelines for Reproductive Toxicity Risk Assessment and Guidelines for Developmental Toxicity Risk Assessment as set forth in 61 FR 56274 et seq. and 56 FR 63798 et seq., respectively.

"Ecology" means the department of ecology.

"Environment" means any plant, animal, natural resource, surface water (including underlying sediments), ground water, drinking water supply, land surface (including tidelands and shorelands) or subsurface strata, or ambient air.

"Environmental half-life" means the time required for the concentration of a chemical to diminish to half its original value. The environmental half-life of a chemical is a measure of a chemical's persistence in the environment.

"Feasible" means reasonably capable of being accomplished or brought about or capable of being utilized or dealt with successfully.

"High-exposure populations" means groups of people that ~~are at greater risk because they~~ [previous phrase struck because equates exposure to risk without consideration of hazard. Generally accepted principal is Hazard X Exposure = Risk.] have a higher potential for exposure than the general population.

"Log-octanol water partition coefficient" or **"Log K_{ow}"** means the ratio of a chemical's concentration in the octanol phase to its concentration in the aqueous phase of a two-phase octanol/water system as expressed in a logarithmic format.

"Low adverse effect concentration" or "LOEC" is the lowest concentration at which an adverse effect is seen in an aquatic toxicity test.

"Media" or **"medium"** means a component of the environment (air, water, soil or sediment) in which a contaminant is measured and an organism lives its life, and from which an organism can accumulate contaminants.

"Neurotoxicant" means a chemical or chemical group that is known or suspected to cause adverse changes in the structure or function of the central and/or peripheral nervous system. For purposes of implementing this chapter, the term neurotoxicant applies to chemicals or chemical groups with sufficient evidence of a neurotoxic hazard in humans or experimental animals consistent with the United States Environmental Protection Agency's Guidelines for Neurotoxicity Risk Assessment as set forth in 63 FR 26926 et seq.

"No observed effect concentration" or **"NOEC"** means the highest concentration of a chemical evaluated in an aquatic toxicity test that does not cause a statistically significant difference in effects compared with controls. [Definition must include that statistical differences are also biologically significant. For example, a study may include measurement of an irrelevant parameter, and find a

statistical difference. That statistical difference does not mean that the so-called 'effect' is biologically significant or a relevant toxicological end point.]

"Persistent, bioaccumulative, and Toxic ~~toxin~~" or **"PBT"** means a chemical or chemical group that meets or exceeds the criteria for persistence, bioaccumulation and toxicity criteria established in WAC 173-33-320.

"Persistence" means the tendency of a chemical to remain in the environment without transformation or breakdown into another chemical form. It refers to the length of time a chemical is expected to reside in the environment and be available for exposure.

"Reference dose" means a numerical estimate of a daily exposure to the human population, including sensitive subgroups such as children, that is likely to be without harmful effects during a lifetime.

"Sensitive population group" means groups of people that exhibit a different or enhanced response to a chemical than most people exposed to a similar level of the chemical because of genetic makeup, age, nutritional status or exposure to other toxic substances.

"Toxicity" means the degree to which a substance or mixture of substances can harm humans, plants or wildlife.

PART III
THE PBT LIST AND CRITERIA AND PROCEDURES FOR REVISING THE LIST

NEW SECTION

WAC 173-333-300 What is the purpose of the PBT list? (1) **Purpose.** The purpose of the PBT list is to identify toxic chemicals that require further action because they remain ("persist") in the environment for long periods of time and ~~where they can~~ bioaccumulate to levels that pose threats to human health and environment in Washington.

(2) **Intended uses of the PBT list.** Ecology will use the PBT list in the following ways: [NOTE: many of these intended uses for a PBT list were included in the Department's previous activities related to penta, octa, and DecaBDE. BSEF provided comments on many of these points at that time.]

(a) **Chemical action plans.** To select chemicals for chemical action plan development.

(b) **Ambient monitoring.** To help guide decisions on the design and implementation of ecology programs for characterizing chemical

concentrations in the ambient environment.

(c) **Biomonitoring.** To encourage and inform the department of health regarding their efforts to monitor chemicals in human tissue.

(d) **Public awareness.** To promote greater public awareness on the problems associated with PBT chemicals, the uses and sources of individual PBTs and steps that individuals and organizations can take to reduce PBT uses, releases and exposure.

(e) **Voluntary measures.** To help identify opportunities for government agencies, businesses and individuals to implement voluntary measures for reducing and phasing out PBT uses and releases.

(3) **Relationship to actions addressing chemical uses and releases.** Ecology has determined that the chemicals on the PBT list pose a potential threat to human health and the environment in Washington.

(a) Ecology's decision to include a particular chemical on the PBT list does not represent a decision that all uses and releases of that chemical should be reduced and phased-out.

(b) Ecology does not intend to use the PBT list as the sole basis for establishing discharge monitoring requirements that are not required under current permits. Ecology will evaluate and, if appropriate, prepare recommendations for additional monitoring requirements when preparing chemical action plans (WAC 173-333-420 and 173-333-430).

NEW SECTION

WAC 173-333-310 What chemicals ~~or chemical groups~~ are included on the PBT list? (1) **Purpose.** This section identifies the chemicals ~~and chemical groups~~ that ecology has determined meet the criteria specified in WAC 173-333-320.

(2) **PBT list.** Ecology has determined that the following chemicals or chemical groups meet the criteria specified in WAC 173-333-320. [NOTE: Many of the listed chemicals are currently regulated under U.S. law. Some are banned in the U.S. Some are available only for restricted uses. Others have been voluntarily withdrawn from production and require prior EPA notification and approval before resumption of production and/or use. Some are not intentionally produced. After quick review that is not intended to be inclusive, those which are banned, voluntarily withdrawn, not intentionally produced or available only for restricted use are marked with a X in the table below.

The additional protective value of this list, beyond the regulations already in place, to the citizens of Washington State should be explained.

Chemicals listed in alphabetical order	CAS Number
Aldrin X	309-00-2
Cadmium	7440-43-9
Chlordane X	57-74-9
Chlordecone (Kepone) X	3734-48-3
Dichlorodiphenyltrichloroethane (DDT) X	50-29-3
Dieldrin X	60-57-1
Endrin X	72-20-8
Heptachlor/Heptachlor epoxide X	76-44-8/1024-57-3
Hexabromobiphenyl X	36355-01-8
Hexabromocyclododecane	25637-99-4
Hexachlorobenzene	118-74-1
Hexachlorobutadiene	87-68-3
Lead	7439-92-1
Mercury	7439-97-6
Mirex X	2385-85-5
Nonylphenol/4-nonylphenol (branched)	25154-52-3/84852-15-3
Pentachlorobenzene	608-93-5
Short-chain chlorinated paraffins	85535-84-8
Tetrabromobisphenol A	79-94-7
Tetrachlorobenzene, 1,2,4,5-	95-94-3
Toxaphene X	8001-35-2
~~**Chemical categories listed in alphabetical order**~~	
Perfluorooctane sulfonates (PFOS)	
Acid	1763-32-1
Ammonium salt	29081-56-9
Diethanolamine salt	70225-14-8
Lithium salt	29457-72-5
Potassium salt	2795-39-3

Phthalate esters	
Di-isodecyl phthalate (DIDP)	68515-49-1 and 26761-40-0
Di-n-hexyl phthalate (DnHP)	84-75-3
Polycyclic aromatic hydrocarbons (PAHs)	
3-Methyl chlolanthrene	56-49-5
7H-Dibenzo(c,g)carazole	194-59-2
Benzo(a)phenanthrene (Chrysene)	218-01-9
Benzo(b)fluoranthene	205-99-2
Benzo(g,h,i)perylene	191-24-2
Benzo(j)fluoranthene	205-82-3
Benzo(k)fluoranthene	207-08-9
Benzo(r,s,t)pentaphene	189-55-9
Dibenzo(a,e)pyrene	192-65-4
Dibenzo(a,h)pyrene	189-64-4
Dibenzo(a,h)acridine	226-36-8
Dibenzo(a,h)anthracene	53-70-3
Dibenzo(a,j)acridine	224-42-0
Fluoranthene	206-44-0
Indeno(1,2,3-cd)pyrene	193-39-5
Perylene	198-55-0
Polybrominated dibenzodioxins and furans X	
2,3,7,8-tetrabromodibenzo-p-dioxin X	50585-41-6
2,3,7,8-tetrabromodibenzofuran X	67733-57-7
Polybrominated diphenyl ethers	
Pentabromodiphenyl ether X	32534-81-9
Octabromodiphenyl ether X	32536-52-0
Decabromodiphenyl ether	13654-09-6
Polychlorinated biphenyls (PCBs) X	
2,3',4,4',5 Pentachlorobiphenyl X	31508-00-6
2,3,4,4',5 Pentachlorobiphenyl X	74472-37-0

2,3,3',4,4' Pentachlorobiphenyl X	32598-14-4
3,3',4,4',5,5' Hexachlorobiphenyl X	32774-16-6
2,3',4,4',5,5' Hexachlorobiphenyl X	52663-72-6
2,3,3',4,4',5' Hexachlorobiphenyl X	69782-90-7
2,3,3',4,4',5 Hexachlorobiphenyl X	38380-08-4
2,3,3',4,4',5,5' Heptachlorobiphenyl X	39365-31-9
Polychlorinated dibenzo-p-dioxins X	
2,3,7,8 Tetrachlorodibenzo-p-dioxin X	1746-01-6
1,2,3,7,8 Pentachlorodibenzo-p-dioxin X	40321-76-4
1,2,3,4,7,8 Hexachlorodibenzo-p-dioxin X	39227-28-6
1,2,3,6,7,8 Hexachlorodibenzo-p-dioxin X	576-53-8
1,2,3,7,8,9 Hexachlorodibenzo-p-dioxin X	19408-74-3
1,2,3,4,6,7,8 Heptachlorodibenzo-p-dioxin X	35822-46-9
1,2,3,4,6,7,8,9 Octachlorodibenzo-p-dioxin X	3268-87-9
Polychlorinated dibenzofurans X	
2,3,7,8 Tetrachlorodibenzofuran X	51207-31-9
1,2,3,7,8 Pentachlorodibenzofuran X	57117-41-6
2,3,4,7,8 Pentachlorodibenzofuran X	57117-31-4
1,2,3,4,7,8 HexachlorodibenzofuranX	70648-26-9
1,2,3,6,7,8 Hexachlorodibenzofuran X	57117-44-9
1,2,3,7,8,9 Hexachlorodibenzofuran X	72918-21-9
2,3,4,7,8,9 Hexachlorodibenzofuran X	60851-34-5
1,2,3,4,6,7,8 Heptachlorodibenzofuran X	67562-39-4
1,2,3,4,7,8,9 Heptachlorodibenzofuran X	55673-89-7
1,2,3,4,6,7,8,9 Octachlorodibenzofuran X	39001-02-0
Polychlorinated naphthalenes	
Trichloronaphthalene	1321-65-9
Tetrachloronaphthalene	1335-88-2

Pentachloronaphthalene	1321-64-8
Hexachloronaphthalene	1335-87-1
Heptachloronaphthalene	32241-08-0

(3) **Lead and cadmium.** Ecology will not develop a chemical action plan for lead and cadmium until the Environmental Protection Agency concludes the development of a metals assessment framework and ecology completes its review of the bioavailability of these two substances.

(4) **Revising the PBT list.** Ecology will periodically review and, as appropriate, revise the PBT list in subsection (2) of this section using the criteria and procedures in WAC 173-333-320 through 173-333-340.

NEW SECTION

WAC 173-333-320 What criteria will ecology use to identify and add chemicals or chemical groups to the PBT list? (1) **Purpose.** This section describes the criteria that ecology will use to determine whether a chemical or group of chemicals should be included on the PBT list.

(2) **Criteria for identifying PBTs.** A chemical or group of chemicals will be included on the PBT list if ecology determines it meets each of the following criteria:

(a) **Persistence.** The chemical or chemical group can persist in the environment based on credible scientific information that:

(i) The half-life of the chemical in water is greater than or equal to ~~sixty~~ 180 days; or

(ii) The half-life of the chemical in soil is greater than or equal to ~~sixty~~ 360 days; or

(iii) The half-life of the chemical in sediments is greater than or equal to ~~sixty~~ 360 days; and Note: The criteria proposed for persistence as those used by the U.S. EPA as screening criteria for use in the evaluation of new chemicals. These half-lives are highly conservative because they are used as *screening* tools in assessing new chemicals. These *screening* criteria are not appropriate for the identification of persistent organic pollutants. Criteria values recommended by ICCA which are indicative of environmental persistence are the half-life of the substance in water (180 days), sediment (360 days) and soil (360 days). (ICCA Briefing Note on Persistent Organic Pollutants, 9/17/98, www.chem.upen.ch/pops/iccappops.htm). Half-lives greater than 60 days, typically 120-180 days for soil and/or sediment, have also been recommended by various international protocols (UNECE 1966, UNEP 2001, EU Guidelines on the Performance

of Risk Assessments).

(b) **Bioaccumulation.** The chemical ~~or chemical group~~ has a ~~high~~ potential to bioaccumulate (Note: A 'HIGH' potential to bioconcentrate is typically defined as a BCF>5000. The primary criterium recommended by ICCA as an indicator of bioaccumulation potential is a fish bioconcentration factor (BCF)>5000. Secondary criteria for non-polar, hydrophobic organic chemicals only is 5<log Kow<7.5, molecular weight<700 and the substance is not metabolized. We recommend reconsideration of the value indicating bioaccumulation in the proposed rule in order to be consistent with criteria developed by other agencies.)based on credible scientific information that the bioconcentration factor or bioaccumulation factor in fish~~aquatic species~~ for the chemical is greater than 1,000 or, in the absence of such data, that the log-octanol water partition coefficient (log K_{ow}) is greater than five provided however, that a chemical may be considered as not bioaccumulative if it has a maximum molecular length of 43 Å, a maximum cross-sectional diameter of 17.4 Å plus a molecular weight of 700-1100, or a measured octanol solubility (mg/L) of < 0.002*MW [NOTE: This definition of 'not bioacculative' was developed as a screening tool by UK and Dutch ecotoxicologists.].
; and

(c) **Toxicity.** [As noted previously, the definition of toxicity when referring to PBT chemicals is restricted to aquatic toxicity.] The chemical ~~or chemical group~~ has the potential to be toxic to humans or ~~plants and~~ wildlife based on credible scientific information that:

(i) The chemical (or chemical group) is a carcinogen, a developmental or reproductive toxicant or a neurotoxicant;

(ii) The chemical (or chemical group) has a reference dose ~~or equivalent toxicity measure~~ that is less than 0.003 mg/kg/day (the basis for this value should be stated); or

(iii) The chemical (or chemical group) has a chronic fish low~~no~~ observed effect concentration (L~~N~~OEC) or equivalent toxicity measure that is less than 0.1 mg/L (unless the water solubility is below this value in which case there is only concern for substances which are toxic below the limits of their saturation) and this concentration is expected to be achieved in the environment for >= 20 days/yr or in the event of environmental occurrence less than 20 days/yr - an acute lethal /effect concentration (LC50 or EC50) ~~no observed effect concentration (NOEC)~~ or equivalent toxicity measure that is less than 1.0 mg/L. [NOTE: these definitions of toxic are consistent with EPA's New Chemicals policy.]

(d) **Additional criteria applicable to metals.** The chemical or chemical group is a metal and ecology determines that it is likely to be present in forms that are bioavailable.

(3) **Degradation products.** Ecology will consider both the chemical and its degradation products when making decisions on whether a chemical meets the criteria in subsection (2) of this section. If a chemical does not meet the criteria in this section for a PBT but degrades into chemicals (in what amounts and at what

rates?) that do meet the criteria in this section for a PBT, the parent chemical will be considered in the development of a CAP for those derivative chemicals.

[Note: Section 173-333-110 states that the purpose of the chapter is to establish the criteria that the Department of Ecology will use to identify persistent bioaccumulative toxicants that pose human health or environmental threats in the State of Washington. The rule creates very objective, measurable values in Section 173-333-320 for persistence, bioaccumulation and toxicity, consistent with what BSEF believes is the intent of the rule: To create a clear standard for designating chemicals as PBTs so that the state can focus its resources on areas of true scientific concern.

Subsection 3 of 173-333-320 (degradation) is inconsistent with this purpose because there is no criteria established for objectively determining what constitutes a level of degradation that should be considered cause for concern. Just as all substances can have toxic effects at a high enough concentration, all substances (save elements) will degrade – to some extent and under some circumstances and in some time periods – into other chemical configurations. If degradation is to be considered, the Department of Ecology should establish clear criteria for identifying and evaluating degradation, including the level of scientific evidence required to show degradation. The Department of Ecology should not be using a proposed rule to arbitrarily add chemicals to the PBT list and thereby circumvent the criteria set forth in Subsection (2), paragraphs a, b, and c of the same section.

NEW SECTION

WAC 173-333-330 What criteria will ecology use to remove a PBT from the PBT list? (1) **Purpose.** This section describes the criteria and factors ecology will use to determine whether a chemical or group of chemicals should be removed from the PBT list.

(2) **Criteria for removing a chemical from the PBT list.** Ecology will remove a chemical ~~or chemical group~~ from the PBT list if the department determines that credible scientific information developed subsequent to the listing decision provides evidence that the chemical or chemical group does not meet the PBT criteria in WAC 173-333-320(2).

NEW SECTION

WAC 173-333-340 What process would ecology follow to revise the PBT list? (1) **Purpose.** This section describes the processes ecology will use to notify the public and amend the PBT list after making a determination that chemicals or groups of chemicals should be added or removed from the PBT list.

(2) **Reviewing and updating the PBT list.** Ecology will periodically review and update WAC 173-333-310. The frequency of review will be determined by credible scientific information available on individual chemicals or chemical groups, rule-making petitions submitted to ecology, and available agency resources. Ecology will comply with the requirements for reviewing and responding to rule-making petitions in the Administrative Procedure Act, chapter 34.05 RCW.

(3) **Public notification.** If ecology makes a preliminary determination that a chemical should be added or removed from the PBT list, the department will prepare a technical discussion paper that summarizes the scientific information supporting the addition or removal of a chemical and notify the public through an announcement posted on the ecology web site and published in the *Washington State Register*.

(4) **Amending the PBT list.** If ecology makes a final determination that a chemical or chemical group should be added or removed from the PBT list, the department will initiate actions to amend WAC 173-333-310 through formal rule making.

PART IV
CHEMICAL ACTION PLANS (CAPs)

NEW SECTION

WAC 173-333-400 What is a chemical action plan (CAP)? A chemical action plan (CAP) is a plan that identifies, characterizes and evaluates uses and releases of a specific PBT or a group of PBTs and recommends actions to protect human health or the environment.

NEW SECTION

WAC 173-333-410 What evaluation factors and processes will ecology use to select PBTs for chemical action plan preparation? (1) **Purpose.** Ecology will consult with the department of health to develop a multiyear schedule for the preparation of chemical action plans. The purpose of this section is to describe the evaluation factors and processes ecology will use to prepare and update the multiyear schedule.

(2) **Evaluation factors.**

(a) Ecology will consider the following factors when preparing the multiyear schedule:

(i) **Relative ranking.** The relative ranking assigned to each PBT based on ecology's evaluation of information on PBT characteristics, uses of the chemical in Washington, releases of the chemical in Washington, the levels of the chemical present in the Washington environment, and levels of the chemical present in Washington residents.

(ii) **Opportunities for reductions.** Whether there are opportunities for reducing or phasing out uses, production or releases of the PBT in Washington. In reviewing available information, the agencies shall consider whether more than one PBT is present in particular products, generated in particular processes or released from particular sources (co-occurring chemicals).

(iii) **Multiple chemical releases and exposures.** Scientific evidence on the combined effects of exposure to one or more PBTs and other substances commonly present in the Washington environment.

(iv) **Sensitive population groups and high-exposure populations.** Scientific evidence on the susceptibility of various population groups including the timing of the exposure and the cumulative effects of multiple exposures.

(v) **Existing plans or regulatory requirements.** Whether there are existing plans or regulatory requirements that reduce and phase out uses and releases of a particular PBT or group of PBTs.

(b) Ecology will not prepare CAPs if the department determines:

(i) All uses and releases of the PBT are prohibited under other state and federal laws or regulations;

(ii) There is credible scientific information to support a conclusion that the PBT is not used, released or present in Washington; or

(iii) There are no available opportunities for reducing or phasing out the uses, releases or exposures of the PBT beyond levels required under other federal or state laws or regulations.

(3) **Preliminary schedule.** Ecology will prepare a preliminary schedule that will identify the PBTs for which CAPs will be developed for the multiyear schedule, the rationale for selecting these PBTs and a timeline for completing CAPs for these PBTs.

(4) **Public notice and comment.** Ecology will notify the public when it has prepared a preliminary schedule and provide an opportunity for public review and comment. Ecology will notify the public through an announcement published in the *Washington State Register* and posted on the ecology web site. Ecology will also send a written announcement to interested persons and organizations. Ecology will provide sixty days, from the date the notice is published in the *Washington State Register* for the public to review and submit comments on the preliminary selection.

(5) **Final schedule.** Ecology will review all public comments on the preliminary schedule prior to preparing a final schedule. Ecology

will notify the public of the final decision through an announcement published in the *Washington State Register* and posted on the ecology web site. Ecology will also provide written notification to individuals or organizations who submitted comments on the preliminary schedule.

(6) **Schedule updates.** Ecology will review and, as appropriate, update the schedule for chemical action plans at least once every three years. In making such revisions, ecology will follow the process for preparing the schedule (including an opportunity for public review and comment) specified in this section.

NEW SECTION

WAC 173-333-420 What are the contents of a CAP? (1) **Contents of the chemical action plans.** Chemical action plans will include, as appropriate, the following types of information, evaluations and recommendations:

(a) **General chemical information.** General information includes, but is not limited to, chemical name, properties, uses and manufacturers.

(b) **Production, uses and releases.** An analysis of information on the production, unintentional production, uses and disposal of the chemical in Washington State. This will include estimates on the amount of each PBT used and released from all sources or activities in Washington and other man-made and naturally occurring sources that may contribute to exposures in Washington. Sources may include other chemicals or products that are known or suspected to degrade to the chemical included on the PBT list.

(c) **Human health and environmental impacts.** Information on the potential impacts on human health and the environment associated with the use and release of the PBT chemical. This will include consideration of available information on the levels of the PBT present in Washington's environment, the likely fate and transport mechanisms, available body-burden data, toxicity effects, and the rates of diseases that have been associated with exposure to the particular PBT.

(d) **Current management approaches.** An evaluation of the regulatory and nonregulatory approaches that influence production, uses, releases and management of each PBT.

(e) **Identification of policy options.** A list of options for managing, reducing and eliminating the different uses and releases of the PBTs addressed in the CAP. The range of options for particular uses and releases will include:

(i) A no-action option;

(ii) An option that results in the elimination of PBT uses and

releases;

(iii) An option to manage chemicals to reduce exposure; and

(iv) Other options, including the use of available substitutes, which will enable full consideration of the opportunities and constraints for reducing particular uses, releases and exposures.

(f) **Recommendations.** Recommendations for:

(i) Reducing and phasing-out uses and releases of the specific PBT or group of PBTs addressed in the CAP;

(ii) Managing products or wastes that contain the specific PBT or group of PBTs addressed in the CAP; and

(iii) Minimizing exposure to the specific PBT or group of PBTs.

The recommendations will be based on an evaluation of the following factors:

(A) Environmental and human health benefits associated with implementing the action;

(B) Economic and social impacts associated with implementing the action;

(C) Feasibility of implementing the action;

(D) Availability, cost and effectiveness of safer substitutes for uses of the PBT being addressed in the plan; and

(E) Consistency with existing federal and state regulatory requirements.

(g) **Implementation steps.** A description of the steps ecology will take to implement the CAP, including a description of:

(i) The existing resources and necessary additional budget ecology intends to use;

(ii) Potential funding sources for CAP implementation, including those that tie implementation costs to PBT sources and products;

(iii) How ecology intends to inform and educate affected persons about the CAP;

(iv) How ecology will promote and assist voluntary actions;

(v) How ecology will collect additional information needed to evaluate the feasibility of potential actions; and

(vi) Any recommended regulatory actions and how ecology will pursue them.

(h) **Performance measures.** A description of interim milestones to assess progress and the use of objectively measurable outcomes, including recommendations for environmental and human health monitoring to measure levels of the chemical(s) (in the CAP) over time.

(i) **Other.** Other information that ecology determines is necessary to support the decision-making process.

(2) **Regulatory consistency.** When evaluating the consistency with existing federal and state regulatory requirements under subsection (1)(f)(iii)(E) of this section, ecology will:

(a) Ensure that the recommendations do not violate existing federal or state laws;

(b) Determine if the recommendations would impose more stringent

performance requirements on private entities than on public entities, unless already required to do so by federal or state law, and if so, describe the justification for doing so; and

(c) Determine if the recommendations differ from federal regulations and statutes, and if so, explain why the difference is necessary and how ecology will coordinate with other federal, state, and local laws applicable to the same activity or subject matter.

(3) **Economic analyses.** In assessing economic impacts under subsection (1)(f)(iii)(B) of this section, ecology will identify costs of implementing the recommendations. This may include a qualitative and/or quantitative analysis of the probable benefits and costs of the CAP.

(4) **Safer substitutes.** When evaluating the availability of safer substitutes for PBT uses, ecology will:

(a) Determine if the recommendations include the use of safer substitutes, and if not, explain why ecology has not recommended this option.

(b) Determine if the recommendations call for additional research for uses with no safer substitutes, and if not, explain why ecology has not recommended this option.

(c) Provide for periodic reevaluation of whether substitutes are available.

NEW SECTION

WAC 173-333-430 What process will ecology use to develop CAPs? (1) **Purpose.** The purpose of this section is to identify the process ecology will use to develop CAPs.

(2) **Workplan/scoping.** Once a chemical is selected for CAP development, ecology will initially plan and scope the CAP of the selected chemical based upon available information regarding the chemical's products, uses and releases; human health exposure and ecological hazards; environmental releases, fate, and transport; environmental concentrations and available substitutes; available options for managing uses and releases; estimated costs, benefits and effectiveness of alternate management options; and any other information ecology determines is necessary to support the CAP development process. Ecology will consult with the department of health regarding all portions of the CAP related to human health exposures.

(3) **Advisory committee.** Ecology will create an external advisory committee for each CAP that ecology develops. The purpose of the advisory committee is to provide stakeholder input and expertise.

(a) The advisory committee membership will include, but not be

limited to, representatives from: Large and small business sectors, community, environmental and public health advocacy groups, local governments, and public health agencies. When appropriate, representatives from the following groups will also be invited to participate: Agricultural groups, worker safety advocacy groups, and other interested parties. Federally recognized tribal governments will also be encouraged to participate. In addition, representation from other state executive agencies may be requested to provide input and to represent agency interests in the CAP development process. Outside experts (if needed) may be requested to provide technical expertise.

(b) A neutral third-party facilitator may be hired to facilitate advisory committee meetings.

(c) The advisory committee will follow a consultative process, where ecology will draft the CAP in consideration of input from advisory committee members.

(d) All advisory committee meetings will be open to the public. Ecology will notify the public of advisory committee meetings through an announcement posted on the ecology web site and written notification to interested individuals and organizations.

(4) **Information collection phase.** Ecology will collect all necessary and up-to-date information regarding the selected chemical. CAP advisory committee members will be asked to contribute, and as appropriate, review information from ecology during this phase of CAP development. The department of health will be asked to review any information related to human health.

(5) **Draft recommendations.** Ecology will develop a draft CAP for advisory committee review and comment. Ecology will review all advisory committee comments and, as appropriate, revise the draft CAP prior to distributing it for public review and comment.

(6) **Public review and comment.** Ecology will notify the public when it has developed a draft CAP and provide an opportunity for public review and comment. The public comment period for each draft CAP will be a minimum of sixty days. Ecology will notify the public through an announcement posted concurrently on the ecology web site, a notice in the *Washington State Register*, and sent to interested persons and organizations. The comment period shall start from the date the notice is published in the *Washington State Register*. During the comment period, ecology will hold a minimum of two public meetings on the draft CAP. One meeting shall be held on the western side of the state, and one meeting shall be held on the eastern side of the state. Ecology may hold additional public meetings during the public comment period if determined necessary. Ecology will provide a response to all public comments.

(7) **Final recommendations.** Ecology will review and provide responses to all public comments on the draft CAP prior to issuing the final recommendations. Ecology will notify the public of the final recommendations through an announcement that will be published in the *Washington State Register* and posted on the ecology web site.

Ecology will also provide written notification to individuals or organizations who submitted comments on the draft CAP.

(8) **Coordination with other agencies.** Ecology will coordinate with other government agencies and interested parties as appropriate on the implementation of the final CAP. Ecology will consult with the department of health on public information materials addressing food safety issues.

I U C L I D

Data Set

Existing Chemical	:	ID: 1163-19-5
CAS No.	:	1163-19-5
EINECS Name	:	bis(pentabromophenyl) ether
EC No.	:	214-604-9
TSCA Name	:	Benzene, 1,1'-oxybis[2,3,4,5,6-pentabromo-
Molecular Formula	:	C12Br10O

Producer related part

Company	:	ALBEMARLE CORPORATION
Creation date	:	26.07.2005

Substance related part

Company	:	ALBEMARLE CORPORATION
Creation date	:	26.07.2005
Status	:	
Memo	:	
Printing date	:	11.11.2005
Revision date	:	
Date of last update	:	24.08.2005
Number of pages	:	90
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	Manufacturer
Name	:	ALBEMARLE CORPORATION
Contact person	:	Dr. Marcia Hardy
Date	:	26.07.2005
Street	:	451 FLORIDA STREET
Town	:	70801 BATON ROUGE, LOUISIANA
Country	:	United States
Phone	:	504-388-8011
Telefax	:	504-388-7686
Telex	:	
Cedex	:	
Email	:	marcia_hardy@albemarle.com
Homepage	:	
Attached document	:	Albemarle Corporation produced this dataset on behalf of, and in conjunction with, the Great Lakes Chemical Corporation (a Chemtura company) and Dead Sea Bromine Corporation (now ICL Industrial Products). The three companies are all manufacturers of DBDPO.
Reliability	:	(1) valid without restriction

19.08.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	bis(pentabromophenyl) ether
Smiles Code	:	c1(Br)c(Br)c(Br)c(Br)c(Oc2c(Br)c(Br)c(Br)c(Br)c2(Br))c1(Br)
Molecular formula	:	C12OBr10
Molecular weight	:	959.17
Petrol class	:	
Reliability	:	(1) valid without restriction

27.07.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	Organic
Physical status	:	Solid
Purity	:	>= 97 % w/w
Colour	:	white powder
Odour	:	None
Attached document	:	Decabromodiphenyl oxide or ether (DBDPO), a solid at room temperature, is a fully brominated (e.g. 10 bromine atoms) diphenyl oxide with a

molecular weight of 959.17 The composition of the commercial product is typically >= 97% DBDPO with the remainder composed of nonabromodiphenyl oxide. DBDPO's measured water solubility (<0.1 ug/L) (Stenzel and Markley 1997) and vapor pressure (4.63 x 10-6 Pa) (Stenzel and Nixon 1997) are negligible. DBDPO's solubility in organic solvents is also extremely low: acetone 0.05%, benzene 0.48%, methylene bromide 0.42%, xylene 0.87%, and 0.2% in toluene (WHO 1994; Norris et al. 1973). DBDPO is often assumed to be lipophilic due its presumed similarity to PCBs (Hardy 2002a). However, no formal fat solubility study has been performed, and pharmacokinetic studies show no appreciable affinity of DBDPO for adipose tissue.

DBDPO is used solely as a flame retardant for the purpose of preventing or delaying ignition in combustible materials . DBDPO's flame retardant activity is derived from its bromine content. Bromine is one of the few elements able to provide flame retardancy in the gas phase; certain plastics require a flame retardant active in the gas phase due to the way they burn. DBDPO's high bromine content makes it very effective as a flame retardant that in turn makes it extremely cost-effective. As a result, DBDPO is the second largest volume brominated flame retardant in production and use. DBDPO's comparative low cost in use alows manuacturers and consumers to reap the benefits of flame retardancy in a variety of end applications.

Global market demand in 1999 for DBDPO was estimated at 54,800 metric tons (BSEF 2001). Market demand, 1999, for DBDPO in the regions of the America's, Europe and Asia was 24,300, 7,500 and 23,000 metric tons, respectively (BSEF 2001). These regional differences reflect differences in the location of end product manufacture. Two companies manufacture DBDPO in the U.S. Production facilities of both manufacturers are located in Arkansas to take advantage of the underground brine fields as a source of bromine.

DBDPO's main application is in high impact polystyrene (HIPS) used for electronic enclosures, e.g. television set cabinet backs (Hardy 2002b). A comparatively minor, but important, use of DBDPO is to flame retard upholstery fabric where it is applied as a fabric back coat encapsulated in latex (Hardy 2002b). DBDPO's potential risk to the consumer, including children, in the upholstery application was recently reviewed by the United States National Academy of Sciences (NAS 2000). DBDPO is not used to flame retard children's clothing or sleepwear.

The DBDPO product is one of three commercial polybrominated diphenyl oxide (a.k.a. ether) products, and historically has accounted for approximately 80% of all polybrominated diphenyl oxide/ether (e.g. "PBDE") production. The other two polybrominated diphenyl oxide/ether products were known as octabromodiphenyl oxide/ether (OBDPO, CAS# 32536-52-0) and pentabromodiphenyl oxide/ether (PeBDPO, CAS# 32534-81-9). Manufacture of OBDPO and PeBDPO was voluntarily disconinued by their sole US manufactuer (Great Lakes Chemical Corporation) in 2004. OBDPO, a mixture of brominated diphenyl oxide congeners ranging from nona- to hexa-, was used to flame retard business equipment constructed of acrylonitrile-butadiene-styrene (ABS) plastic. PeBDPO, a highly viscous liquid composed of tetra-, penta- and hexaBDPO congeners, was used to flame retard flexible polyurethane foam that is used as cushioning in upholstery. Neither OBDPO nor PeBDPO were used to flame retard textiles.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
15.08.2005

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Benzene, 1,1'-oxybis[2,3,4,5-pentabromo

Reliability : (1) valid without restriction
03.08.2005

DBDPO

27.07.2005

Deca

Reliability : (1) valid without restriction
27.07.2005

Decabromodiphenyl ether

27.07.2005

Decabromodiphenyl oxide

27.07.2005

FR-1210

Reliability : (1) valid without restriction
19.08.2005

Great Lakes DE-83R

19.08.2005

SAYTEX 102E Flame Retardant

19.08.2005

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name :
Molecular formula :
Value :

Attached document : The composition of the commercial product is typically >= 97% DBDPO with the remainder composed of nonabromodiphenyl oxide.

The DBDPO commercial product has been analyzed for trace quantities of 15 2,3,7,8-substituted polybrominated-p-dibenzodioxins (PBDD) and dibenzofurans (PBDF) under a U.S. Environmental Protection Agency (EPA) test rule. None of the analytes were present at or above the quantitation limits established by the agency (Ranken et al. 1994).

Resins containing DBDPO have also been analyzed for PBDD/PBDF content. A high impact polystyrene (HIPS) resin containing antimony trioxide and DBDPO was molded using normal (215-220?C; 30 sec.), abusive (235-245?C; 5 min.) or extreme (265-270?C, 7 min.) processing conditions (McAllister et al. 1990). The molded resin was cryogenically ground and analyzed for six 2,3,7,8-substituted PBDD/PBDFs. None were detected. Polybutyleneterephthalate (PBT) resin containing antimony trioxide and DBDPO was also molded under similar conditions, and analyzed. No 2,3,7,8-substituted PBDD/PBDFs were detected. Donnelly et al. also analyzed molded HIPS/DBDPO/Sb2O3 and molded PBT/DBDPO/Sb2O3, and detected no 2,3,7,8-TBDF and no 1,2,37,8-PeBDF. Brenner and Knies (1990) also reported no PBDDs in their analysis of an extruded PBT/DBDPO blend.

Virgin molded HIPS/DBDPO/Sb2O3 and repeatedly ground and injection molded (e.g. "recycled") HIPS/DBDPO/Sb2O3 resins meet the requirements of the German Chemicals Banning Ordinance with respect to 2,3,7,8-substituted PBDD/F content (Hamm 1999; Hamm et al. 2001). The concentrations of relevant PBDD/F congeners were at least one order of magnitude below the regulated limit values for PBDD/F (1 ppb for the sum of four congeners, 5 ppb for the sum of all eight regulated congeners).

15.08.2005 (1) (2) (3) (4) (5)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling : no labelling required (no dangerous properties)
Specific limits :

Reliability : (1) valid without restriction
29.07.2005

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :

Reliability : (1) valid without restriction
29.07.2005

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : Industrial
Category : Polymers industry

Attached document : DBDPO is used solely as a flame retardant for the purpose of preventing or delaying ignition in combustible materials. DBDPO's flame retardant activity is derived from its bromine content. Bromine is one of the few elements able to provide flame retardancy in the gas phase; certain plastics require a flame retardant active in the gas phase due to the way they burn. DBDPO's high bromine content makes it very effective as a flame retardant that in turn makes it extremely cost-effective. DBDPO's comparative low cost in use alows manuacturers and consumers to reap the benefits of flame retardancy in a variety of end applications. As a result, DBDPO is the second largest volume brominated flame retardant in production and use. Global market demand in 1999 for DBDPO was estimated at 54,800 metric tons (BSEF 2001). Market demand, 1999, for DBDPO in the regions of the America's, Europe and Asia was 24,300, 7,500 and 23,000 metric tons, respectively (BSEF 2001). These regional differences reflect differences in the location of end product manufacture.

Two companies manufacture DBDPO in the U.S. Production facilities of both manufacturers are located in Arkansas to take advantage of the underground brine fields as a source of bromine.

DBDPO's main application is in high impact polystyrene (HIPS) used for electronic enclosures, e.g. television set cabinet backs (Hardy 2002b). DBDPO is also used in electrical wire and cable insulation and electrical connectors. A comparatively minor, but important, use of DBDPO is to flame retard upholstery fabric where it is applied as a fabric back coat encapsulated in latex (Hardy 2002b). DBDPO's potential risk to the consumer in the upholstery application was recently reviewed by the United States National Academy of Sciences (NAS 2000). DBDPO is not used to flame retard children's clothing or sleepwear.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
15.08.2005 (6) (7)

Type of use : industrial
Category : Textile processing industry

Attached document : DBDPO is used solely as a flame retardant for the purpose of preventing or delaying ignition in combustible materials.

DBDPO's main application is in high impact polystyrene (HIPS) used for electronic enclosures, e.g. television set cabinet backs (Hardy 2002b). DBDPO is also used in electrical wire and cable insulation and electrical connectors. A comparatively minor, but important, use of DBDPO is to flame retard upholstery fabric where it is applied as a fabric back coat encapsulated in latex (Hardy 2002b). DBDPO's potential risk to the consumer in the upholstery application was recently reviewed by the United States National Academy of Sciences (NAS 2000). DBDPO is not used to flame retard children's clothing or sleepwear.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
15.08.2005 (6) (8)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis

Type : Production

15.08.2005

1.8 REGULATORY MEASURES

Type of measure :
Legal basis : other: US National Academy of Sciences

Attached document : U.S. National Academy of Science Oral Reference Dose

The U.S. National Academy of Sciences (NAS) was asked by the U.S. Congress to evaluate the consumer risk of flame retardants that could be used to meet CPSC's proposed standard for upholstered furniture. The evaluation was published in the document "Toxicological Risks of Selected Flame-Retardant Chemicals" which is available on-line at www.nap.edu (NAS, 2000). DBDPO was one of the flame retardants evaluated (See pages 72-98 of that report).

An oral reference dose (RfD) of 4 mg DBDPO/kg/d was calculated by NAS (NAS 2000). A reference dose is that dose to which humans, including the most sensitive groups, can be exposed daily over the course of a lifetime with the expection of no effects.

NAS derived an oral RfD for DBDPO by using the chronic (2 year) NOAEL of 1,120 mg/kg-d, based on liver thrombosis and degeneration observed in rats at the next higher dose in the NTP carcinogencity bioassay (NTP 1986), and a composite uncertainty factor of 300, resulting in an RfD of 4 mg/kg-d (RfD = NOEL + 300). In the IRIS Database, the U.S. EPA gives a reference dose (RfD) of 1 x 10-2 mg/kg-d for DBDPO based on the 1 mg/kg-d NOAEL for histopathology and other toxicity endpoints in rats exposed via diet for 2 yr (Kociba et al. 1975). The Kociba study used a test article which was only 77% DBDPO, and is thus not relevant to today's product. Doses higher than 1 mg/kg-d were not tested in the Kociba study, precluding identification of a LOAEL. The reason the NTP (1986) 2-yr toxicology/carcinogenesis bioassay for DBDPO was not considered in the current IRIA risk summary (EPA 1999) is because the NTP results were not available at the time of the risk derivation (1984-1985).

In all scenarios evaluated by NAS, dermal, oral or inhalation exposure to DBDPO did not present a risk of adverse health effects to the consumer, including children mouthing upholstery textiles. The WHO (1994) and the European Union also concluded the general population is at negligible risk from DBDPO.

Reliability : (1) valid without restriction
15.08.2005 (9) (7) (10) (11)

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other: ACGIH Workplace Environmental Exposure Level (WEEL), TWA
Limit value : 5 mg/m3

Reliability : (1) valid without restriction
15.08.2005 (12)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : other: TSCA, EINECS, MITI
Additional information :

Reliability : (1) valid without restriction
15.08.2005

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

Type : degradation product
CAS-No :
EC-No :
EINECS-Name :
IUCLID Chapter :

Attached document : See Sections 3.1.1, 3.1.2, 3.8.
Reliability : (1) valid without restriction
16.08.2005

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

Memo : Fires Are a Serious Problem.

Attached document : Fires are a serious problem (Aherns 2003). The U.S. has one of the highest fire incidence and mortality rates of all developed countries. This is despite all modern efforts including fire departments, building codes, fire drills, fire sprinklers, fire extinguishers, UL ratings, and flame retardants.

The National Fire Protection Association (Karter 2003) reports that in the the United States in 2002:

· Every 19 seconds, a fire department responded to a fire somewhere in the United States.

· Public fire departments attended 1,687,500 fires, of which 519,000 occurred in structures, 329,500 occurred in vehicles, and 839,000 occurred in outside properties.

· Nationwide, there was a civilian (non-firefighter) fire death every 156 minutes. There were 3,380 fire deaths, a decrease of 9.8% from the previous year, excluding the events of 9/11/01.

· About 79% of all fire deaths occurred in home fires. There were

2,670 deaths from fires in the home, a decrease of 14.1% from the previous year.
· Nationwide, there was a civilian fire injury every 28 minutes. There were an estimated 18,425 civilian fire injuries, of which 14,050 occurred in homes.

NFPA concluded that fire safety initiatives targeted at the home are key to any reductions in overall fire death toll, because 79% of all civilian fire deaths there (Karter 2003). One of the five recommendations made by NFPA to reduce these deaths was to seek additional ways to make home products more fire safe. The wider use of upholstered furniture and mattresses that are more resistant to cigarette ignitions was cited as an example of change that has "already accomplished much and will continue to do more".

Intentional fire setting is the leading cause of fires, fire deaths and direct property damage in non-residential structure fires.

Basic Fire Facts

Fire is dark. In television and movies, fire is often portrayed as a bright light, but the fire environment is actually pitch black due to the dense smoke produced. Escape plans must be memorized (USFA 2002; Education World 2002).

Smoke from fire kills. Fire victims typically succumb to smoke inhalation before flames reach them. More fire deaths occur when people are sleeping-between 2 a.m. and 6 a.m (USFA 2002; Education World 2002).

Many people believe - falsely - that they would awaken in a fire. But toxic gases, typically carbon monoxide, actually put people into a deeper sleep (USFA 2002; Education World 2002).

Fire is intensely hot. This might seem obvious, but few realize that fire can cause the temperature to rise several hundred degrees in seconds. That degree of heat can cause the human body to stop functioning and a loss of consciousness, making escape impossible (USFA 2002; Education World 2002).

Fire is fast. A home can be completely consumed by fire in less than five minutes. In less than 30 seconds a small flame can get completely out of control and turn into a major fire. It takes only minutes for thick black smoke to fill a house. Time is the biggest enemy and every second counts (USFA 2002; Education World 2002).

Flame retardants prevent or delay ignition, reduce the rate of heat release, reduce the quantity of toxic gases generated, and increase the time available for escape. Flame retardants can increase escape time by a factor of 15. In a fire where every second counts, this can literally mean the difference between life and death.

01.08.2005 (13) (14) (15) (16)

Memo : Groups at High Risk of Death and Injury in Fires

Attached document : Populations at high-risk of death, injury or burns in fires are the very young, the elderly, and the economically disadvantaged (NFPA 2003; NSKC 2004; Stevens and Mann 1999). Children ages 5 and under, who represent 9 percent of the population but more than 17 percent of all fire-related deaths in the home, are more than twice as likely to die in a fire as the rest of the population. A child's risk of dying in a fire is twice the national average. Adults 65 and older also face a risk twice the average, while people 85 and

older had a risk that is almost four-and-a-half times more than average. Home fires and home fire-related deaths are more likely to occur during cold-weather months, December through March. The South has the highest fire-related death rate in the country, 21 percent higher than the national rate. Home cooking equipment is the leading cause of residential fires and fire-related injuries. However, residential fires caused by smoking materials (e.g., cigarettes) are the leading cause of fire-related death and the third leading cause of fire-related injury.

Reliability : (1) valid without restriction
03.08.2005 (8) (17) (18)

Memo : Children Are at Special Risk in Fires

Attached document : Fires and burns are the fifth leading cause of unintentional injury-related death among children ages 14 and under. Children, especially those ages 5 and under, are at the greatest risk from home fire-related death and injury, with a fire death rate more than twice the national average. A less acute perception of danger, less control over their environment, and a limited ability to react promptly and properly to a fire contribute to this excess risk (NSKC 2004). In 2001, 493 children ages 14 and under died in residential fires. Nearly 54 percent of these children were ages 4 and under. Each year, nearly 40,000 children ages 14 and under are injured by fires in the home. More than 70 percent of all fire-related deaths are from smoke inhalation, caused by toxic gases produced as fires develop and spread. Burns are responsible for an additional 25 percent of fire-related deaths. Smoke inhalation alone accounts for more than half of all fire-related injuries to children ages 9 and under.

The majority of fire deaths and injuries occur in homes without a working fire alarm while the residents are asleep. A working smoke alarm is not present in two-thirds of the residential fires in which a child is injured or killed. Children in homes without smoke alarms are at greater risk of fires and fire-related death and injury. Almost 55 percent of children ages 5 and under who die from home fires are asleep at the time, while nearly one-third of these children are too young to react appropriately.

Children playing with fire account for 5 percent of residential fires, yet cause 40 percent of residential fire-related deaths among children. More than half of all child-play home fires begin in a bedroom, often while children have been left alone to play. Roughly three out of five of these fires are started by children playing with matches or lighters.

The number of candle-related fire deaths, most caused by candles left unattended or inadequately controlled increased 20 percent between 1998 and 1999, hitting a 20-year peak. A child playing with or near a candle is one of the leading contributors to candle-related fires.

Male children have a higher rate of fire-related death and injury than female children. Studies indicate that by age 12, half of all children have played with fire. Males are nearly twice as likely as females to have played with fire. Children from low-income families are at greater risk for fire-related death and injury, due to factors such as a lack of working smoke alarms, substandard housing, use of alternative heating sources and economic constraints on providing adequate adult supervision. Children living in rural areas have a dramatically higher risk of dying in a residential fire. Death rates in rural communities are more than twice the rates in large cities and more than three times higher than rates in large towns and small cities. Black children are more than twice as likely as white children to die in a fire. More than 43 percent of residential fire-related deaths among children ages 9 and under occur when the child is attempting to escape, unable to act or acting irrationally. Although an escape plan may help to reduce these deaths, only 25 percent of households have developed and practiced

a plan. People with a physical or cognitive disability are more than twice as likely to die in a house fire. Limited mobility may interfere with a child's ability to escape, and cognitive impairments may interfere with a child's awareness of imminent danger.

The total annual cost of fire- and burn-related deaths and injuries among children ages 14 and under is more than $11.9 billion. Children ages 4 and under account for more than $4.1 billion of these costs.

01.08.2005 (19)

Memo : Flame Retardants - Protection Through Prevention

Attached document : Years ago, most combustible building contents were made of cellulosic materials commonly found in nature (Leihbacher 1999). Chairs and tables were made of wood, sofas and bedding with cotton batting and jute, carpeting with wool and cotton fibers, and draperies with linen and other natural materials. Rapidly spreading fires were uncommon and generally indicated the use of a petroleum-based accelerant like gasoline. Today, the furnishings in homes and businesses include those constructed of petrochemicals such as polyurethane foams and rigid polystyrene plastic. These materials can behave in a fire as if they have built-in-accelerant, and can produce quantities of heat exceeding those of ordinary combustibles.

Another change from the past is that today's buildings and homes have more contents. The fire load in residential structures has more than doubled in the past 50 years on a pound per square foot basis (Leihbacher 1999). Flashover, when the room bursts into flame and the most dangerous time of a fire, has become more common as a result of the greater fire load and the use of synthetic furnishings. Synthetics, especially foams and plastics, produce more heat than natural products - the heat produced by burning foams and plastics can approach that of highly volatile flammable liquids. This contributes to the development of flashover so that flashover now occurs rapidly - generally within 3-10 minutes after ignition. Flashover signals the change from a contents to a structure fire and the beginning of the structural collapse danger.

Another change in modern buildings and homes is increased energy efficiency (Leihbacher 1999). Buildings are designed to hold heat inside in the winter and exclude heat in the summer. Over the last 20 years new energy-efficiency standards have come into effect, and better and more insulation of walls, floors, ceilings, roofs, and windows has occurred. This higher energy efficiency influences the building's behavior during a fire. Energy efficient upper walls and ceilings are less able to conduct heat away from the fire room, resulting in a higher temperature fire in the room of origin. Energy efficient thermal pane windows are less likely to break and vent the fire's heat outdoors than older window types. In the event of a fire, the net result of enhanced energy efficiency is rooms that burn hotter and hold heat better.

The combination of higher energy efficiency and a greater quantity of synthetic materials increases the potential for a serious fire if ignition occurs (Leihbacher 1999). Thus, the extensive use of synthetic polymers has intensified the need and concern for flame retardancy in many applications. Flame retardants are especially useful in flammable foams and plastics where they act to delay ignition and slow flame spread. Flame retarded products, once ignited, generate a lower rate of heat release which slows development of flashover. A slower rate of heat release also lowers the quantity of toxic gases produced. These factors translate into longer escape times for occupants - the use of flame retardants can increase escape times by a factor of 15 (FRCA 1987; Babrauskas et al. 1988) - and save lives (Clarke 1997).

The benefits of brominated flame retardants (BFRs) in the U.S., in terms of lives saved, were determined using fire data from the National Fire Protection Association (NFPA) (Clarke 1997). Four product classes were identified in which BFRs are widely used and which could be directly associated with fire data: television/appliances, wire/cable insulation, curtains/draperies and upholstered furniture. Based on this data, an estimated 190 lives are saved annually through the use of BFRs (e.g. DBDPO) in television cabinets. For electrical insulation and draperies, less product and fire data were available, but 80 and 10 lives, respectively, were estimated saved annually through the use of BFRs in these products. Again, DBDPO is a major flame retardant used in electrical insulation and in draperies. Thus, an estimated 280 deaths are avoided each year in the U.S. due to the use of BFRs. A large portion of these lives saved are likely attributable to DBDPO. Another 140-220 fire deaths per year could be avoided if upholstered furniture fabrics were backcoated with BFR-latex as is now done to meet California standards for upholstered furniture.

1 Flashover is caused by the radiation feedback of heat. Heat from the growing fire is absorbed into the upper walls and contents of the room, heating combustible gases and furnishings to their auto-ignition temperature. This build up of heat in the room triggers flashover. Flashover signals the end of an effective search and rescue in a room; it means the death of any person trapped in the blazing room - either civilians or firefighters.

01.08.2005 (20) (21) (22) (23)

Memo : The Bottom Line

Attached document : Someone in the U.S. dies in a fire about every two and half hours. Most of those deaths are in the home. Those dying are typically the very young, the very old, and the economically challenged. The total cost of fire in the U.S. is estimated at $186-305 billion depending on whether the events of September 11 are included. According to NFPA (Hall 2003): "The conclusion that fire has a tremendous impact on the way the U.S. uses its scarce resources is indisputable." And "It also is clear that we have a dual interest in reducing U.S. fire losses - which include human losses that are among the highest per capita in the industrial world - and in seeking ways to achieve equivalent fire safety at lower costs, since the growth in total cost of fire has been led not by the fire losses but by the other cost components. This provides a clear indication of need for product innovations or other programs (e.g., educational) that can improve fire safety at the same or lower costs. It also shows the need for improved methods (e.g. models) for calculating fire performance and costs, so the implications of different choices can be considered and judged more comprehensively."

01.08.2005 (24)

1.12 LAST LITERATURE SEARCH

Type of search : External
Chapters covered :
Date of search : 07.08.2005

15.08.2005

1.13 REVIEWS

Memo : Hardy M. 2002a. The toxicology of the three commercial polybrominated

diphenyl oxide (ether) flame retardants. Chemosphere 46, 757-777.

01.08.2005

Memo : Hardy M. 2002b. Properties of the major commercial PBDPO flame retardant, DBDPO, in comparison to comparison to PBB and PCB. Chemosphere 46, 717-748.

01.08.2005

Memo : Not recommended: Darnerud et al. Polybrominated diphenyl ethers: occurence, dietary exposure, and toxicology. Environmental Health Perspectives 109:49-67 2001.

Attached document : The Darerud et al. paper is not recommeded, becuase it proposes a LOAEL of 1 mg/kg/d for all "PBDEs" based on the pentabromodiphenyl ether product. A LOAEL of 1 mg/kg/d is not appropriate for DBDPO for which a NOAEL of at least 1000 mg/kg/d was recommended (Hardy 2000a). The EU risk assessment utilized a NOAEL for DBDPO of 1120 mg/kg/d based on the NTP two year study in rats and mice (NTP 1986).

03.08.2005

03.08.2005

2.1 MELTING POINT

Value	:	= 304 °C
Sublimation	:	
Method	:	
Year	:	1999
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	TGA analysis of the commercial DBDPO product indicates 50% weight loss at 389 degrees C and 90% weight loss at 408 degrees C.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (25)

2.2 BOILING POINT

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .0000000463 hPa at °C
Decomposition	:	
Method	:	
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO's vapor pressure was determined to be 4.63 x 10-6 Pa using the spinning rotor guage.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (26)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 6.265 at 25 °C
pH value	:	
Method	:	other (measured): OPPTS 830.7560
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO's partition coefficient was determined to be 6.265 using the generator column method.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (27)

Partition coefficient	:	octanol-water
Log pow	:	= 12.61 at °C
pH value	:	
Method	:	other (calculated):EPIwin v3.4
Year	:	
GLP	:	no
Test substance	:	other TS
Attached document	:	DBDPO's estimated octanol-water partition coefficient appears to be a better predictor of its behavior in biological systems than its measured value, based on mamallian pharmacokinetic studies and fish bioconcentration data. This is likely due to DBDPO's very poor solubility in both water and octanol so that any small change in concentration produces a large change in its measured Log Kow value.
Reliability	:	(1) valid without restriction

03.08.2005 (28)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	< .0001 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	insoluble (< 0.1 mg/L)
Stable	:	
Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO's water solubility was determined using the generator column method.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (29)

Solubility in	:	Organic Solvents
Value	:	< .01 - .87 vol% at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Attached document	:	DBDPO's solubility in organic solvents is extremely low: <0.01% in acetone and methanol, 0.76% in toluene, bezene 0.48%, methylene bromide 0.42%, and xylene 0.87% (Albemarle Corporation 1999; WHO 1994; Norris et al. 1973). DBDPO is often assumed to be lipophilic due its presumed similarity to PCBs (Hardy 2002a). However, no formal fat solubility study has been performed, and pharmacokinetic studies show no appreciable affinity of DBDPO for adipose tissue. Using NTP's (1986) pharamacokinetic data,

DBDPO's blood:liver:adipose ratio in the rat was 1:7:2 compared to Arochlor 1254's ratio of 1:22:359 as reported by Kodavanti et al. 1998.

01.08.2005 (25) (30) (31) (11)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : DBDPO Physical/Chemical Properties

Attached document : DBDPO has negligible water solubilty and vapor pressure. It is poorly soluable in in organic solvents. It is a stable molecule.

03.08.2005

3.1.1 PHOTODEGRADATION

Type	:	other
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight

Attached document :

Degradation of Deca in the environment has been suggested as a potential source of tetra, penta and hexaBDEs. Scenarios have been proposed that Deca breaks down during processing, is metabolized by fish or mammals, or is degraded by light or microbes. However, results of laboratory and field monitoring studies do not support the hypothesis that Deca is a significant source of these PBDEs (see section 3.8 for a discussion these studies).

Photolytic degradation of Deca to lower brominated diphenyl ethers has been studied by many research groups (Eriksson et al. 2004; Soderstrom et al. 2004; Hua et al. 2003; Barcellos de Rosa et al. 2003; Watanabe et al. 1987). Deca's low aqueous solubility (<0.1 µg/L) has frustrated attempts to directly study its breakdown in that media. Attempts using water/organic solvent mixtures have also been largely unsuccessful. For example, Erikkson et al. (2004) were unable to detect any degradation products of Deca in water, and suggested that Deca's disappearance from the solution may have been due to adsorption to the glass walls of the vessel. As a consequence, most photolysis studies have utilized organic solvents, where Deca has limited solubility. When tested in organic solvents, natural and artificial sunlight cause the small amount of Deca in solution to undergo reductive debromination, ultimately, to diphenyl ether. During this process, lower brominated diphenyl ethers are some of the many substances formed as intermediates, and some of the components of the Penta and OctaBDE commercial products, plus other PBDEs, have been reported on a qualitative basis (Bezarea-Cruz et al. 2004). However, these temporarily formed PBDEs were not those commonly found in environmental samples, and because of this Söderström et. al. concluded that the Penta mixture, and not degradation of Deca, was the most likely source of the tetra-, penta- and hexaBDEs found in the environment (Soderstrom et al. 2004). In addition, these studies indicate that all of the PBDEs, including BDE-47, 99 and 100, will undergo reductive debromination when in solution in organic solvents, with the rates proportional to the number of bromines on the aromatic rings.

Nevertheless, photolysis studies performed in organic solvents are unlikely to be applicable to Deca's environmental fate. Early in its development as a commercial product, it was recognized, based on other halogenated aromatics, that Deca's photolysis would likely proceed by different routes in water and organic solvents (Norris et al. 1974, 1975). In solvents capable of proton transfer, halogenated aromatics typically degraded by reductive dehalogenation; however, in water, oxidation led to the formation of phenolic compounds. Further, once photohydroxylation was initiated in water, its rate was expected to accelerate as electron-withdrawing halogens were replaced by electron releasing hydroxyl groups. The resulting hydroxylated species were expected to adsorb light more strongly and this ultimately could result in rupture of the aromatic ring. Laboratory findings correlated with the predictions. Only minimal evidence of Deca's (98% purity) aqueous photodegradation was found over a 3-month exposure to natural sunlight, and the degradants were not lower brominated diphenyl oxides. Evidence for degradation of only 0.57% of the amount initially present (10 g/8 l water) was detected after 98 days of exposure to sunlight. However, Deca (7 ppm) in octanol decomposed with a half-life of 4 h. In xylene, a strong absorber of UV light, Deca

photodegraded by reductive debromination with a half-life of 15 h on exposure to a 125 watt Hg lamp.

In air, Deca is expected to be associated with particulate matter, rather than in the gaseous phase, because of its low vapor pressure (4.63 x 10-6 Pa) and high adsorption coefficient (1.8 x 106). Deca deposited on dust (silica particles), suspended in dry air, and irradiated with artificial sunlight was found to be photoinert; no measurable degradation to PBDEs occurred (Zetch 2003).

Söderstrom et al. (2004) reported that irradiation of Deca deposited on moist sand, silica gel, sediment or soil resulted in slow formation of unidentified products as well as PBDEs of differing composition from those commonly found in the environment. BDE-47, 99 and 100 were not detected after irradiation of soil, sand or sediment, and these researchers concluded that Deca was not the source of the tetra and pentaBDEs typically detected in the environment. In their concluding paragraph, they said "In this investigation the most commonly found PBDEs in environmental samples (BDE 47, BDE 99 and BDE 100) were only formed to a minor degree from the photolysis of DecaBDE and only in toluene and/or on silica gel. BDE 153 was formed in toluene, on sand outdoors and on sediment. The origin of these congeners in the environment is probably primarily from emission of technical PentaBDE products and possibly from other degradation pathways of DecaBDE. To further investigate the degradation pathways of decaBDE, combined photolytic/bacterial degradation pathways should be examined."

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
16.08.2005 (32) (33) (34) (35) (36) (37) (38) (39) (40)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C

Attached document : DBDPO is not expected to undergo hydrolysis based on its chemical structure. DBDPO's negligible water solubility (< 0.1 ug/L) and limited partitioning into water precludes hydrolysis as a significant route of environmental degradation.

03.08.2005

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement : concentration at contaminated site
Media : sediment
Concentration :
Method :

Attached document : Zweidinger et al. (1978) analyzed sediment near a U.S. DBDPO manufacturing site. Levels ranged from N.D. to 14,000 ug/kg. The detection limit was ~ 100 ug/kg.

DBDPO was detected at 13 µg/kg in a sample of surface sediment from a

sediment core collected from the western basin of Lake Ontario (Alaee 2001).

The Great Lakes receive input from urbanized, industrialized and agricultural areas along their shores. Zhu and Hites (2005) estimate a total PBDE content in the 5 Great Lakes' sediment of about 100 tons. Deca makes up about 95-99% of the PBDE sediment total. Using BSEF's 1999 figure of a market demand in the America's (includes US, Canada and South America) of 24,300 or 48,600,000 kg of Deca, then the total Deca content in Great Lakes sediment is approximately 0.0039-0.004% of only one year's market. This sediment value represents all Deca deposited since first manufactured.

La Guardia et al. (2003) reported detection of DBDPO in North Carolina freshwater sediments downstream from a wastewaste water treatment plant whose influent contained DBDPO. The wastewater treatment plant received influent from a site using DBDPO in a textile application, and DBDPO was detected in the treatment plant's influent and effluent. Levels in the effluent were substantially lower (~96%) than the influent (note that EPiwin, v3.4, predicts approximately 94% of DBDPO in an influent will be removed by a sewage treatment plant. See Section 3.3.1). DBDPO content in the sediment peaked (293,774 ug/kg total organic carbon) within 0.5 miles of the wasterwater treatment plant discharge into the stream. This is consistent with the prediction that DBDPO would not move far in the environment from its point of release. The site using DBDPO in a textile application had historic releases to wastewater treatment that peaked in 1994 with substantial reductions of approximately 93% beginning in 1999. This study is frequently cited as providing evidence of DBDPO's degradation. However, the paper provides no evidence to this effect and did not reach this conclusion.

Oros et al (2005) reported no detectable DBDPO in sediment samples derived from the San Francisco estuary (D.L. < 1.5 ng/g dry wt).

16.08.2005 (41) (42) (43) (44)

Type of measurement : background concentration
Media : other:sewage sludge
Concentration :
Method :

Attached document : Hale et al. (2001a) reported detectable levels of DBDPO in some sewage sludge samples collected from four different regions in the U.S. DBDPO concentrations were variable and ranged from < 75 to 9,160 ug/kg dry wt. Hale et al. (2001b) reported also reported varying levels of DBDPO (84.8 - 4890 ug/kg dry weight) in 11 samples of sludge collected in New York, Maryland, Virgina and California. Eight of the samples contained less than 600 ug/kg while 3 contained approximately 1400 - 4800 ug/kg dry weight. DBDPO was also detected in sewage sludge (1,470 ug/kg dry wt) collected from a sewage treatment plant located in a region of the U.S. where DBDPO-treated upholstery textiles are manufactured (Hale et al. 2002).

In some parts of the U.S., sewage sludge undergoes further treatment and is then applied to agricultural soils as a fertilizer. Thus, DBDPO could be present in soils used for agricultural purposes and the potential for its uptake into food crops or by grazing farm animals is considered. No studies have evaluated the potential for uptake of DBDPO by plants, but studies have demonstrated that DBDPO is not toxic to 6 species of terrestrial plants (Porch and Krueger 2001) or to earthworm survival or reproduction (Aufderheide et al. 2001). DBDPO's potential for uptake by plants can be evaluated based on its physical/chemical properties, data on related compounds, and plant physiology.

Although DBDPO data is not available, information is available on polybrominated biphenyl (PBB) plant uptake and translocation. No detectable PBB was found in plants collected from the 10 most highly contaminated fields in Michigan, U.S. (Jacobs et al. 1978). Autoradiograms of corn and soybean seedlings grown in the presence of 14C-PBB showed no translocation (Chou et al. 1978). PBB was found associated with the roots of these plants, but due to the insolubility of PBB in water, the PBB was primarily associated with the root surface (e.g. physically adsorbed to the root's surface). The amount of PBB associated with (not absorbed by) three root crops (onions, radishes, carrots) grown in two PBB-contaminated soils of differing organic matter and clay content ranged from 0 to a maximum of 0.5% of the soil concentration (Chou et al. 1978).

Three root crops, radishes, carrots, and onions, were grown in two PBB-contaminated soils of differing organic matter and clay content (Chou et al. 1978). No PBB uptake was found, but trace amounts of PBB were associated with the edible portions of each crop (Table 5-3). No PBB were associated with the roots of radishes, carrots or onions grown in high organic carbon soil contaminated with 100 ppb PBB. A maximum of 0.5% of the soil concentration was found in carrots grown on low organic carbon soils contaminated with 100,000 ppb PBB; high organic soil reduced the association to 0.1% of soil concentration. The authors concluded these trace amounts were probably associated with root surfaces, because Iwata et al. (1974) found 97% of polychlorinated biphenyl (PCB) residues in carrot roots in the peel and similar results were reported previously for DDT and other organochlorine pesticides in the soil in which carrots were grown.

Radishes grown in a garden (estimated PBB concentration = 500-1000 ppb) located in a heavily contaminated field (500-1000 ppb) did not contain PBB. Chou et al. concluded: "From these results plus our previous results of greenhouse and field studies in which we found no PBB in plant tops, we conclude that little if any PBB will be transferred from contaminated soil to plant tops. Thus, recontamination of animals from feeds grown in contaminated soil will likely not occur. Although some root crops from very highly contaminated soil might contain traces of PBB, much of this PBB could probably be removed by peeling."

TABLE 5-3. PBB found associated with radish, carrot, and onion roots after 6, 9, and 10 weeks, respectively, of growth in PBB contaminated soil. Detection limit = 0.3 ppb.

Soil Type	PBB Added to Soil (ppb)	PBB in plant roots (ppb)		
	Radishes	Carrots	Onions	
Loamy Sand(Low Carbon)	100	7	20	ND
	100,000	49	535	63
Clay Loam(High Carbon)	100	ND	ND	ND
	100,000	44	117	34

Plants may be a source of exogenous chemicals via retention by root surfaces, root uptake and translocation, and foliar uptake. Transfer to animal tissues can occur via soil and herbage ingestion (Wild and Jones 1992). "Assuming degradation of the compound does not occur within the plant, and plant root uptake and translocation of organic chemicals from the soil is passive, plant uptake can be described as a series of consecutive partition reactions. Partitioning occurs between soil solids and soil water, soil water and plant roots, plant roots and transpiration stream, and transpiration stream and plant stem. This partitioning can be related to the octanol:water partition coefficient, such that compounds with high log Kow values (e.g. PAHs, PCBs, PCDD/Fs) are most likely to be sorbed by the

soil and/or plant root. Chemicals with lower Kow values are likely to be translocated within the plant and may reach the above ground portions of the plant."

Wild and Jones (1992) go on to state "Relatively few studies have investigated the plant uptake of organic compounds from sludge-amended soils. However, some general comments can be made from the studies: (a) to date studies have been confined to relatively few groups of compounds, namely PCB, PAHs and some other organochlorines; (b) these compounds are generally not taken up into the above-ground portion of crop plants; (c) there is some evidence of slight enrichment of some compounds in some root crops, but the transfers are very inefficient, and consequently the BCFs are very low. Generally enrichments are confined to the root peels which are normally removed before consumption; (d) it is worth noting that the studies to date have focused on compounds which, because of their physico-chemical properties, are thought less likely to be transferred efficiently into crop plants. Future studies should focus on semi-volatile compounds of intermediate log Kow, and some polar compounds."

Based on the screening approach of Wild and Jones (1992), which uses log Kow to predict plant uptake, DBDPO is predicted to have high adsorption to soil, low volatilization from soil, low degradation in soil, low potential for leaching, high retention by root surfaces, low potential for root uptake and translocation, low potential for foliar uptake, high potential for transfer to animal tissues by soil ingestion and low potential for transfer to animal tissues by foliage ingestion.

This screening approach identifies two possible routes of exposure to DBDPO following application of sewage sludge to agricultural soil: retention on root surfaces and transfer to animal tissues by soil ingestion. Based on DBDPO's log Kow, adsorption to root surfaces appears likely. Although it seems likely that DBDPO could adsorb to root surfaces and thereby be ingested, DBDPO's known poor absorption from the gastrointestinal tract (<0.3-2% of the oral dose), makes potential for systemic exposure very low. Similarly, the potential for transfer to animal tissues by soil ingestion is based on the soil half life and log Kow, and does not does not take into account actual animal absorption data. Since DBDPO is known to poorly absorbed from the gastrointestinal tract (<0.3-2% of the oral dose), the potential transfer of DBDPO to animal tissues by soil ingestion is therefore low.

In summary, based on the screening approach of Wild and Jones (1992) and PBB plant uptake data (Chou et al. 1976; Jacobs et al. 1978; Iwata et al. 1974) DBDPO is expected to sorb to root surfaces if present in soil, but not to be transferred into the interior of the root. The amount of DBDPO available for adsorption to roots is expected to be some fraction of the total soil content due to extensive binding to soil particles (Koc = 1.796 x 10+6). DBDPO is not expected to be absorbed into the root nor is it expected to be transferred to foliage. Based on pharmacokinetic data, mammalian uptake of DBDPO after ingesting root crops would be < 0.3-2% of the oral dose. Thus, exposure to DBDPO as a result of its presence in agricultural soils due to the application of sewage sludge is expected to be insignificant.

15.08.2005 (45) (46) (47) (48) (49) (50) (51)

Type of measurement : background concentration
Media : air
Concentration :
Method :

Attached document : Sampling over a 3 year period (1997-1999) at 4 locations on the shores of the Great Lakes detected DBDPO only at trace levels in the Chicago filter

samples. The average concentration over the three years in the Chicago area was 0.3 pg/m3 and ranged from 2.0×10-7 µg/m³ to 3.5×10-7 µg/m³ (Strandberg et al. 2001). These trace levels were only detected in the particulate, and not the gas, phase. DBDPO was not detected in any of the three years in samples collected from the shores of Lake Superior and Lake Erie, and a site on Lake Michigan farther north than Chicago (D.L. = 0.1 pg/m3). The authors concluded that due to DBPDO's physical chemical properties, DBDPO is strongly bound to particles and will therefore not travel far from its source. This is consistent with Wania and Dugani's (2002) conclusion that DBDPO will not travel far from its point of release and has little potential for long range transport.

Samples of dust and smoke aerosols that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC were collected 5 or 6 days after September 11, 2001 were analyzed for a wide variety of components including volatile/semivolatile organic compounds, metals, polychlorinated dioxins and furans, polychlorinated biphenyls and PBDEs. DBDPO was detected in all three samples ranging in concentrations from 1,330 to 2,660 ug/kg dry weight (Lioy et al 2002).

04.08.2005 (52) (53) (54)

Type of measurement : background concentration
Media : food
Concentration :
Method :

Attached document : Due to its poor bioavailability, poultry, meat and dairy products are not expected to be significant exposure source of DBDPO. Limited monitoring data is available. DBDPO concentrations were not above background levels (0.87 ng) in most samples of chicken fat (n=13) collected from four different areas of the U.S.; matrix and laboratory blanks contained low, but detectable, levels of DBDPO. Tetra- (0.56-10.58 ng/g), penta- (0.42-16.97 ng/g), and hexaBDE (0.02-4.63 ng/g) congeners were generally present at 3-100 times the background. Mono- to deca-brominated congeners were not detected in chicken feed or its ball clay additive (Huwe et al. 2002).

Fish consumption is not expected to be a source of human exposure to DBDPO. A recent time trend and spatial distribution of Great Lakes fish did not detect DBDPO (Zhu and Hites 2004). According to the authors "The amounts of BDE-209 found in all fish samples were in the range of 'undetectable' to 3.6 ng, which was the same level as the blanks; thus, we could not conclude that BDE-209 was present in any of these samples." The time trend covered was from 1980 to 2000. The Great Lakes sampled were Superior, Michigan, Huron, Erie and Ontario. Lake trout, a top salmonid predator, were the fish sampled in all lakes, except Lake Erie where only walleye were avaiable. Similarly, DBDPO was not detected in a large study (n~700) of farmed and wild salmon (Hites et al. 2004; Hardy 2004).

Several additional studies have analyzed U.S. fish samples for DBDPO. Only one study reports detecting DBDPO in fish collected in the U.S. (see Table below). DBDPO has negligible water solubility (<0.1 ug/L) and in the environment will preferentially partition to soil and sediment. Thus, any exposure to fish via water will be extremely low. Further, DBDPO has been shown not to bioconcentrate in fish (CITI 1992; Kierkegaard et al. 1997, 1999; Stapleton et al. 2004). Bottom feeding species could conceivably be exposed to DBDPO-containing sediment. However, limited uptake by these species is expected due to DBDPO-sediment binding and DBDPO's large molecular weight and size. (Supporting this is the fact that no uptake of DBDPO from soil by earthworm was detected. See Section 4.8.) Thus, any exposure to humans via fish would be extremely limited.

TABLE. Analytical results of freshwater fish collected in U.S. waters for DBDPO content.

Species & Year Collected	Location	DBDPO Level	# Samples	Ref
Various	3 Lakes, US, 2000	N.D. (D.L. = 1.5 ng/g wet wt)	20	Dodder
Carp	River, US, 1991	N.D. (D.L. = 0.1 ug/kg wet wt)	48	Loganathan
Salmon	Alaska, 2000*	N.D. (D.L. = 0.65 pg/g wet wt)	2	Easton
Minnows	N.C., 2002	N.D.	63	La Guardia
Sunfish	N.C., 2002	492 ng/g lipid	13	La Guardia

*DBDPO was also not detected in 6 samples of wild or farmed salmon or fish-food collected in Canada in 2000. D.L. = 0.65 pg/g wet wt.

DBDPO was also not detected in bivalves collected in the San Francisco estuary in 2002 (Oros et al. 2005).

Schecter et al. (2004) reported analyzes of US foods in a market basket survey of 30 food types from three major supermarket chains in Dallas, TX. Food samples were almost exclusively foods of animal origin: meat, fish, and dairy products. Thirteen PBDE congeners were measured in each sample. BDEs 47 and 99 predominated. DBDPO was reported as detected in one catfish fillet, calf and chicken liver, cheese and margerine. These results should be interpreted with caution given the much larger studies reporting nondetectable levels of DBDPO.

16.08.2005 (55) (56) (57) (58) (59) (60) (61) (43) (62) (63)

Type of measurement : other
Media : surface water
Concentration :
Method :

Attached document : Oros et al. (2005) reported detecting DBDPO in water collected in 2002 from the San Francisco estuary. The range was from below the detection limit to 191 pg/L or ppq. DBDPO was most abundant in water collected in the Lower South Bay area. This region of the estuary receives approximately 26% of the estuary's total publicly-owned-treatment-works wastewater effluents and only 10% of the estuary's freshwater infow. It also has a shallow water depth, is surrounded on 3 sides by urban area, is minimally flushed by tides, and receives significant quantities of urban runoff. The PBDEs detected in water were partitioned into the suspended particulate matter. Despite detection of trace levels in some water samples, DBDPO was not detected in sediments or in bivalves collected in the estuary.

15.08.2005 (43)

Type of measurement : background concentration
Media : biota
Concentration :
Method :

Attached document : See the record relating to Food for information regarding DBDPO's detection, and lack thereof, in fish.

Eggs of marine and freshwater bird species from British Columbia, Canada, were analyzed for PBDE content (Elliott et al. 2005). The dominant PBDEs in all birds were 47, 100, 99, 153 and 154. A subsample

of the eggs were analyzed at higher resolution, and DBDPO was reportedly detected in the range of 0.9-1.8 ug/kg ww in osprey. DBDPO was not detected in great blue heron, double crested cormorant or Leach's storm petrel eggs.

08.08.2005 (64)

Type of measurement : background concentration
Media : other: household dust
Concentration :
Method :

Attached document : House dust and clothes dryer lint have been analyzed for DBDPO content. House dust samples collected from homes in the Washington D.C. metropolitan area were analyzed for 22 PBDEs (Stapleton et al. 2005). The dominant congeners observed were those associated with the penta and DBDPO products. No correlations were observed with the year of house construction, type of flooring (i.e., hardwood vs carpet) or the number of television sets or personal computers in the home. DBDPO was typically the dominant congener detected in house dust, although concentrations were highly variable (median 1350 ng/g dry mass; range 162-4310 ng/g dry mass). Dryer lint from 5 of the homes were also analyzed; DBDPO was detected in all five.

Schecter et al (2005) reported detection of DBDPO in wipe samples from 4 computers and in 7 out of 9 vacuum dust samples. DBDPO is not used to flame retard computers; thus, the most likely source of the DBDPO reported is air-borne dust.

Both these studies (Stapleton et al. 2005; Schecter et al. 2005) suffer from lack of standardization in vacuuming techique, failure to record frequency of dusting/vacuuming/other cleaning techniques, lack of information on ventilation rates and other variables known to effect air-borne particulates (RIVM 2004); Lioy 2002; Wallace et al. 2004; Thatcher and Layton 1995). Different vacuum methods can show very large differences in sampling efficiencies and can lead to high variability between samples. Most vacuum cleaners do not trap small (<20 um) particles and will simply re-enter them in to the air. The cleaning frequency can also lead to high variability between samples. DBDPO is associated with particulates, and factors which affect particulates can be expected to contribute variability in measured vales.

The Environmental Working Group (EWG) recently published a report on levels in house dust collected from 10 homes across the U.S. DBDPO was detected in the dust in concentrations ranging from N.D. to 7510 ng/g (ppb). As is typical of EWG reports, the document was short on facts. The methodology section of the report consisted of the following: "We asked ten women from the breast milk study to collect samples of dust from their homes. These participants were selcted to be a representative sample of the original group with respect ot geographical location, PBDE body burden, age and occupation. Women who had moved since submitting their breast milk samples were excluded from the follow-up study. No one reported occupational exposure to foam or plastics, except the use of computers in onan office setting. The ten study participants vacuumed their house as they normally would and sent EWG either the dust bag from their vacuum cleaners or, if they owned vacuum cleaners without bags, emptied the cartridge of their machine into a clean zip-lock bag. The women also filled out a questionaire on the model and make of their vacuums, how many times they had used their machine since last changing the bag or emptying the canister, and the number of rooms in their house with carpet. Samples were sent to a certified laboratory for analysis." This study also suffers from a lack of standardization. Comparison of the results between the 10 individual homes or with other

studies is therfore inappropriate.

16.08.2005 (65) (66) (67) (68) (69) (70) (71)

Type of measurement : background concentration
Media : other: human
Concentration :
Method :

Attached document : A few studies have analyzed U.S. human adipose tissue, serum, hair or breast milk for the presence of DBDPO.

Responses were noted that corresponded to qualitative criteria for hexa- through octabromodiphenyl oxide congeners in adipose tissue collected from the general U.S. population in fiscal year 1987. This adipose tissues was collected as a part of the National Human Adipose Tissue Survey (NHATS 1990). A subsequent study analyzed selected composites from the 1987 NHATS repository (Cramer et al. 1990; Stanley et al. 1991). The presence of hexa- through octabromo congeners was confirmed, and nonabromo- and DBPDO were also identified. DBDPO was detected in 3 of the five extracts analyzed. The concentrations ranged from N.D. to 700 pg/g adipose.

Twelve samples collected in 1988 from a general population of U.S. blood donors in the Midwest were analyzed approximately 10 years later for DBDPO content. DBDPO concentrations in the serum ranged from <1 pmol/g lipid to 35 pmol/g lipid (equivalent to < 0.96 ng/g lipid to 33.6 ng/g lipid) (Sjödin et al. 2001b). Only five of the twelve samples were above the limit of quantification (LOQ = 1 pmol/g lipid).

Out of three composite hair samples collected in a barbershop (floor sweepings) located in the vicinity of DBDPO manufacture, one composite had a DBDPO concentration of 5 µg/kg, and a second had a low level of DBDPO detected, but not quantified (DeCarlo 1979).

DBDPO has only recently been reported in breast milk. DBDPO is not expected to be transferred to breast milk in significant quantities based on its physical/chemical properties, pharmacokinetics and the physiology of milk production.

Schecter et al. (2003) analyzed 47 samples of breast milk collected from women in Austin or Dallas, TX for 12 PBDPO/PBDE isomers. A subset of those samples (n=23) was also analyzed for DBDPO. Sixteen (70%) of these 23 samples had no dectectable level of DBDPO. Seven were reported to contain DBDPO levels ranging form 0.48 - 8.24 ng/g lipid (ppb). The mean DBDPO level was 0.92 +/- 1.96 ng/g lipid. DBDPO represented approximately 1% of the mean total PBDPO/PBDE content.

The Environmental Working Group analyzed 20 samples of breast milk collected from women in the U.S (EWG 2004). The samples were analyzed for 44 different PBDPO/PBDE isomers. Thirty-five isomers were detected. The mean DBDPO level was 0.24 ng/g lipid and ranged from 0.08 to 1.23 ug/kg lipid. The standard deviation was not reported. DBDPO represented approximately 0.15% of the mean total PBDPO/PBDE content.

This limited dataset indicates DBDPO represents < 1% of the total PBDPO/PBDE content in breast milk collected in the U.S. The mean DBDPO level detected in these two studies, 0.92 or 0.24 ng/g lipid, is far below all estimates derived under DBDPO's Voluntary Children's Chemical Evaluation Program (VCCEP 2002; Hays et al. 2003). In these scenarios, the worst-case exposure estimate was derived for a mother of a breast-feeding infant assumed to work in the bagging operation at a DBDPO manufacturing site. The calculated daily intake for an infant exposed via

breast milk ranged from 1.9×10-2 to 3.4×10-1 mg/kg-day for the Reasonable (RE) and Upper Estimate (UE), respectively. This is far below the Reference Dose of 4 mg/kg/d derived for DBPDO by the National Academy of Sciences. A Reference Dose is that exposure to which all populations, including the most sensitive, could be repeatedly exposed without expectation of adverse effects.

16.08.2005 (72) (73) (74) (75) (76) (77) (78) (79)

Type of measurement : other
Media : other
Concentration :
Method :

Attached document : Section 3.2.1 Environmental Monitoring primarily focuses on data specific to the U.S. and Canada. Additional data may be availble in some matrixes collected in other parts of the world. DBDPO's environmental partitioning is consistent irrespective of country. For a short summary of DBDPO's environmental detection including areas outside the US up until 2000, see Hardy (2000). For an in-depth review of DBDPO's environmental detection that includes later data, see the EU risk assessment.

Reliability : (1) valid without restriction
Flag : Risk Assessment

16.08.2005 (80) (81)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other
Year :

Attached document : DBDPO is predicted to partition in the environment to soil and sediment (~99%) where it will bind extensively to organic carbon (estimated Kocsoil = 1.67 x 1012) and to be essentially immobile in soil. Based on a release of 1,000 kg/hr to air, water and soil, the predicted partitioning is: air 0.12%, water 1.09%, soil 41.8% and sediment 57% (Level III Fugacity Model, EPIwin V3.04). The majority (73%) would be reacted in soil and sediment, with only 23% of the total undergoing advection. DBDPO is not expected to volatilize from water based on its river and lake volatilization half-lives and air-water partition coefficient. DBDPO is expected to partition from water to organic carbon. Sewage treatment plants are predicted to remove DBDPO from the influent to a high degree (94%), but biodegradation in the treatment plant is not expected. Removal in the treatment plant is via partitioning to sludge. DBDPO leaching from polymers was insignificant (Norris et al. 1973,1974) as expected for a molecule of negligible water solubility and vapor pressure.

DBDPO is not expected to undergo long range transport. A preliminary evaluation of DBDPO's potential for long-range transport in the atmosphere indicated that this was unlikely (Hardy and Smith 1999). Wania and Dugani (2002) recently concluded extensive computer modeling of the

long-range transport potential of DBDPO. Four multimedia models were used: Characteristic Travel Distance, Spatial Range, Arctic Accumulation Potential, and Globo-POP. All four models produced similar results, and Wania and Dugani concluded that DBDPO was unlikely undergo long-range transport. Instead, DBDPO released to the environment would deposit near the point of release. This behavior was very different from that predicted by the models for brominated diphenyl oxides having 2-4 bromine atoms/molecule. The Di- to TetraBDE molecules were predicted to have a long range transport potential similar to chlorinated biphenyls with 4-6 chlorine atoms/molecule known to undergo significant long-range transport.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
02.08.2005 (82) (31) (83) (54)

3.3.2 DISTRIBUTION

01.08.2005

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum :
Deg. product :
Method : other: MITI
Year : 1992
GLP :
Test substance : other TS: 14C-DBDPO

Attached document : Ready Biodegration (MITI)

DBDPO (100 mg/l) was incubated with activated sludge (30 mg/l) from mixed sources in Japan over a 2-week period (equivalent to MITI I test). No degradation (as measured by BOD) was observed; therefore DBDPO is not readily biodegradable (CITI, 1992). This result indicates that DBPDO is unlikely to biodegrade rapidly in the environment under aerobic conditions.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
15.08.2005 (84)

Type : anaerobic
Inoculum : other: freshwater sediment
Concentration : 5 related to Test substance
500 related to Test substance
Contact time : 8 month
Degradation : (±) % after
Result : under test conditions no biodegradation observed
Deg. product : no
Method : other
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : 32 Week Anaerobic Sediment Degradation Study

The anaerobic biodegradation of 14C-DBDPO was studied in a sediment-water system over 32 weeks at 5 or 500 mg/kg sediment (Schaefer and Flaggs, 2001a). 14C-Glucose served as a positive control. The test article was a mixture of unlabelled substance (supplied as a composite sample from three manufacturers; purity 97.4% DBDPO, 2.5% NonaBDPO and 0.04% OctaBDPO) with 14C-DBDPO (radiochemical purity 96.8%). This study was conducted according to Good Laboratory Practices.

The sediment and accompanying overlying surface water used was collected from the Schuykill River, Valley Forge, Pennsylvania, USA. The redox potential of the sediment was 284 mV. The average moisture content of the sediment was 26%, its pH was 6.3, and the organic matter content was 1.4%. A 0.2 mg/l resazurin solution was prepared using the collected overlying surface water.

The test chambers consisted of 500 ml bottles containing 300 ml of the sediment and were prepared in an anaerobic chamber. The sediment was carefully added to the bottles in order to maintain the sediment column structure. Three replicate chambers were used at each concentration. In addition, a further six treatment groups at 5 mg/kg and 500 mg/kg were run to allow the concentrations of the test material and any metabolites to be determined at the start and end of the test. The test chambers were incubated in the dark at ambient room temperature (22oC) in an anaerobic chamber. At the end of the incubation period, samples from each treatment group were analysed for DBDPO and the presence of any degradation products by a HPLC method using both UV and radiometric detection.

For the positive control, an average of 95% of the total radioactivity added as glucose was recovered with 85% converted to 14CO2 and 14CH4 and 10% associated with the sediment-phase. The degradation seen in the positive control indicated that the sample pre-treatment methods (e.g. use of tetrahydrofuran solvent) appeared to have had little effect on the viability of the microbial community present.

For DBDPO, <1% of the total radioactivity added was found as 14CO2 and 14CH4 indicating that essentially no mineralisation occurred. Parent compound analysis (mean of seven replicate samples) indicated that the concentrations of DBDPO in the nominal 5 mg/kg treatment were 6.64 ± 0.70 mg/kg at day 0 and 6.51 ± 2.15 mg/kg at week 32. Similarly, the measured concentrations of DBDPO in the nominal 500 mg/kg treatment were 543 ± 77 mg/kg at day 0 and 612 ± 158 mg/kg at week 32. The differences in concentration between day 0 and week 32 were not statistically significant. The composition of the sediment cores were found to account for some of the variability seen in the measured concentrations, with sediments containing a greater number of gravel/stones leading to a higher variability between replicate measurements of concentration.

The HPLC chromatographic profiles also indicated that traces of some 14C-labelled components with shorter retention times than DBDPO were present in some of the 32-week samples in the 5 mg/kg treatment group. Similar components also were present in the stock solution of the 14C-DBDPO. A more detailed GC-MS analysis was carried out on Day 0 and Week 32 sediment samples. No evidence for the formation of lower brominated congeners was found.

A similar anaerobic degradation study was performed with 2,2',4,4'-TetraBDE (Schaefer and Flaggs, 2001c). The substance tested was a mixture of 14C-2,2',4,4'-TetaBPE (radiochemical purity 96.5%) and unlabelled 2,2',4,4'-TetraBDE (purity ~99%). The test concentrations were 5 and 500 mg/kg dry sediment. A positive control (14C-Glucose) was also run. The test was carried out using the same sample preparation method, a

similar sediment and the same test system as used for DBDPO.

The total recovery of 14C from the positive control was 101%, with 81.2% converted to 14CO2 and 14C, and 19.6% associated with the sediment-phase. The degradation seen in the positive control indicates that the sample pre-treatment methods using tetrahydrofuran solvent appear to have had little effect on the viability of the microbial community present.

Under the conditions of these studies, neither DBDPO nor 2,2',4,4'-TeBDE were found to degrade in anaerobic sediment over a period of 32 weeks.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (85) (86) (87)

Type : anaerobic
Inoculum : other: sediment
Contact time : 2 year
Degradation : (±) % after
Result : under test conditions no biodegradation observed
Deg. product : no
Method : other
Year : 1994
GLP : no data
Test substance : other TS

Attached document : 2 Year Anerobic Sediment Degradation Study

KEMI (1999) and de Wit (2000) reported that no degradation/transformation of DBDPO was seen after four months incubation in sediment samples under anaerobic conditions. The inoculum used was an enrichment culture from a polybrominated diphenyl oxide-contaminated sediment. The incubation of one of the anaerobic cultures was extended to two years, but no degradation of decabromodiphenyl ether was seen. De Wit (2002) stated, "A study of anaerobic microorganisms' ability to break down DeBDE to lower brominated PBDE in sediment was carried out during 1994. DeBDE was applied to anaerobic sediment which was then inoculated with micro-organisms enriched from a PBDE-contaminated sediment. The sediment was then divided into smaller samples and allowed to gently shake. Samples were analyzed at different time points but no breakdown of DeBDE was seen during the experimental time of four months. The experiment was extended by letting one aliquot of sediment continue incubation. Subsamples were analyzed at several time points but no breakdown could be seen after an incubation of 2 years (unpublished results, Ulla Sellström; de Wit,1995; 1997)."

Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (88) (89)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 48 hour(s) at °C
Concentration : 20 µg/l
Elimination :
Method : other
Year : 1973
GLP : no data

Test substance : other TS: 14C-DBDPO

Attached document : 48 Hour Fish Bioconcentration Study with Comparison to Tetrachlorobiphenyl

The bioconcentration of 14C-DBDPO (20 ug/L) in rainbow trout under static conditions over a 48-hour period was compared to a known bioaccumulative substance, 2,2',4,4'-tetrachlorobiphenyl (TCBP) (16 ug/L). Little change in the DBDPO water concentration was seen in the water (initial concentration was 20 µg/l), indicating minimal uptake by the trout and insignificant losses by other means (e.g. volatilisation, adsorption onto surfaces etc.). DBDPO's lack of bioconcentration was confirmed by analysis of 14C-residues in fish samples at intervals during the experiment. Little or no uptake of DBDPO occurred. The positive control, TCBP, was found to bioconcentrate at least 50 times over the initial exposure levels within 4 hours. DBDPO did not bioconcentrate under the conditions of this study, whereas TCBP was shown to bioconcentrate (Norris et al. 1973,1974).

Reliability : (1) valid without restriction
03.08.2005 (31) (83)

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 42 day(s) at °C
Concentration : 6 µg/l
BCF : < 50
Elimination :
Method : other
Year : 1992
GLP :
Test substance : as prescribed by 1.1 - 1.4

Attached document : 6 Week Fish Bioconcentration Study

The bioconcentration of DBDPO in carp was studied over a six-week period in a study performed according to Japan's "Bioaccumulation test of chemical substance in fish and shellfish" (CITI 1992). The 48 hr LC50 was first determined in orange-red killifish (Orizias latipes), and the value was used along with the analytical detection limit of the test substance to select two test concentrations for the bioconcentration test in Japanese carp (Cyprinus carpio). Concentrations used in this design are typically 1/100, 1/1000 or 1/10,000 of the 48 hr LC50. The highest exposure concentration was 10 times that of the low exposure concentration. For DBDPO, the test concentrations were 6 and 60 ug/L. The control and test groups consisted of 15-20 fish each. The duration of exposure was 6-8 wks until equilibrium was reached in the fish. Test article concentrations in the aquaria and fish were determined twice/wk, and in 2-3 treated fish/exposure concentration every 2 weeks. The control fish were analyzed before test initiation and at termination of exposure for the test substance. The whole body of each fish was homogenized and extracted using an analytical method suitable for the test substance. Test article concentrations in fish and water were corrected for analytical recovery rates. Analytical method blanks were also performed. The BCFs measured at the end of the experiment were <5 at an initial concentration of 60 µg/l and <50 at an initial concentration of 6 µg/l (the two values are consistent if no DBDPO was detected in the fish, and the detection limit in fish was around 300 µg/kg, and indicate that little or no bioconcentration is occurring) (CITI, 1992).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (90)

Species : Oncorhynchus mykiss (Fish, fresh water)
Exposure period : 120 day(s) at °C

Concentration	:	
Elimination	:	
Method	:	other
Year	:	1997
GLP	:	no
Test substance	:	other TS

Attached document : 120 Day Dietary Fish Bioaccumulation Study

Kierkegaard et al. (1997, 1999) investigated the uptake in trout of Dow FR-300-BA following administration in food. The Dow product has not been manufactured since the 1980s, contained only 77.4% of the DBDPO isomer with the remainder being nona- (21.8%) and octaBDPO isomers (0.8%) (Norris et al 1973, 1974, 1975). However, Kierkegaard et al. did not provide the composition of the mixture tested.

Rainbow trout were force-fed homogenized cod containing the suspended test article for a period of 16, 49 and 120 d. Doses ranged between 7.5 and 10 mg/kg/d. Only a very small amount of the test material was taken up during the 120-day exposure phase. Uptake was estimated to be 0.02 - 0.13% of the dose after 120 days of exposure based on the muscle concentrations of the total hexa- to DBDPO isomers. Uptake of the DBDPO component was estimated at only 0.005% of the dose, and declined significantly during depuration. No evidence of debromination of the test article to 2,2',4,4'-TeBDPO, 2,2',4,4',5-PeBDPO or 2,2',4,4',6-PeBDPO was found, and the authors concluded "... possible metabolism seem not to be the major sources of tetra- and pentabromodiphenyl ethers found in wild fish".

Some hexa-, hepta-, octa- and nonaBDPO congeners' concentrations increased with exposure in liver and muscle. Some of these congeners were not detectable in the test article and Kierkegaard et al. speculated that their presence might be the result of a metabolic process or a more efficient absorption of trace amounts initially present in the food/test article. Kierkegaard et al. was not able to distinguish between these two possibilities. A third possibility, not considered in Kierkegaard et al., is that these hexa-, hepta-, octa- and nonaBDPO congeners were present in the test article but not detected, and slowly increased in fish tissue over time to detectable levels over the 120 d test period as a result of slow metabolism/elimination.

This study, along with Stapleton et al. (2003) are frequently cited as evidence that DBDPO is "bioavailable" and metabolized to lower brominated diphenyl ethers. These conclusions fail to take into account that uptake of DBDPO was estimated at only 0.005% of the dose, and that this indicates an exceedinglly low "bioavailability". These conclusions overlook that the main PBDEs detected in biota, BDE47, 99, and 100, were not reported as "metabolites", and that the authors concluded that DBDPO's "...possible metabolism seem not to be the major sources of tetra- and pentabromodiphenyl ethers found in wild fish".

Reliability : (4) not assignable
15.08.2005 (91) (92) (93)

Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	90 day(s) at °C
Concentration	:	
BCF	:	= 0
Elimination	:	
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	other TS

Attached document : 90 Day Fish Bioaccumulation Study

Stapleton et al. (2003) fed juvenile carp food containing BDE 209 for 90 consecutive days (940 ng BDE 209/day/fish). No uptake of BDE 209 was demonstrated; no BDE 209 was detected in fish at a detection limit of ~1 ng/g wet weight. A 0.4% bioavailability of BDE 209 over the 90-day course of the study was estimated beased on detection of presumed metabolites.

Negligible absorption is consistent with previous laboratory studies in rats and fish and with the lack of bioaccumulation indicated by environmental monitoring. It is so low as to present no hazard or risk. Seven lower brominated diphenyl ether congeners were detected in the fish, and their detection was attributed to metabolic debromination of BDE 209. The 7 lower brominated congeners ranged from penta- to octaBDE congeners, and do not match those reported in wild caught fish. Fifty to seventy percent of the total PBDEs in wild caught fish is typically represented by 2,2',4,4'-TetraBDE (BDE 47). The congener present in the next highest amounts is typically 2,2',4,4',5-PentaBDE (BDE 99) followed by 2,2',4,4',6-PentaBDE (BDE 100). This is not the pattern of isomers reported by Stapleton et al., and does not support their implied conclusion that the penta and HexaBDEs detected in wild caught fish derive from BDE 209. It is also significant that Stapleton et al. did not detect nonaBDPEs in fish tissues. If BDE 209 were being selectively debrominated in fish tissue, one would expect to find at least some nonabromoDPE. The results of this bioaccumulation study are consistent with previous work showing insignificant bioconcentration of DBDPO in fish, do not provide evidence that DBDPO is debrominated metabolically, and indicate that metabolic debromination of DBPDO is not the source of tetra- and pentaBDPO congeners detected in wild-caught fish.

This paper, along with Kierkegaard et al., is frequently cited as evidence that DBDPO is bioavailable and metabolized to lower brominated diphenyl ethers. These conclusions do not, however, take into account that no DBDPO was detected in the fish fed treated food for 120 days. Nor do these conclusions take into account that DBDPO's uptake by fish was estimated, based on presumed metabolites only, to be 0.02-0.13% of the entire 120 day dose. These facts indicate an exceedingly low bioavailability. Further, the presumed metabolites detected do not match the lower brominated diphenyl ethers typically found in biota.

Reliability : (4) not assignable
15.08.2005 (94) (95)

3.8 ADDITIONAL REMARKS

Memo : Decabromodiphenyl Oxide (Ether): A Discussion of Its Potential for Biological or Physical Degradation to Lower Brominated Diphenyl Ether Congeners

Attached document : Polybrominated diphenyl ether (PBDEs) flame retardants have received worldwide attention following their detection in the environment. The PBDEs most frequently detected are specific isomers with 4, 5, and 6 bromine atoms (BDE-47, 99, 100, 153 and 154) and appear to originate from the pentabromodiphenyl ether product (Penta) (Ikonomou et al. 2002; Wilford et al 2003). The Penta product was used to impart flame retardancy to flexible polyurethane foam, primarily used in upholstered furniture. The principal components of Penta, 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) and 2',2',4,4',5-pentabromodiphenyl ether (BDE-99), are typically the dominant PBDEs found in aquatic, terrestrial and atmospheric compartments. Decabromodiphenyl oxide/ether (Deca; BDE-209) (CAS#

1163-19-5) manufacture has constituted over 80% of the global production of PBDEs and will approach 100% with the termination of Penta and Octa production by the sole manufacturer, Great Lakes Chemical Corporation, at the end of 2004. Deca's applications are very different from that of Penta and do not overlap. Deca is used to flame retard styrenic resins intended for electrical and electronic applications. Deca's primary applications in the United States are in television cabinet backs molded from high impact polystyrene and in wire and cable insulation. A secondary use is as a flame retardant backcoat for upholstery textiles (but not in upholstery foam cushions, the Penta product is the PBDE used in that application).

Degradation of Deca in the environment has been suggested as a potential source of tetra, penta and hexaBDEs. Scenarios have been proposed that Deca breaks down during processing, is metabolized by fish or mammals, or is degraded by light or microbes. However, results of laboratory and field monitoring studies do not support the hypothesis that Deca is a significant source of these PBDEs.

A study of the thermal behavior of Deca showed that Deca is extremely stable under the processing conditions used commercially for its incorporation into high impact polystyrene. The concentrations of tri- through hepta-BDEs remained constant before and after a normal extrusion/injection molding cycle. After repetitive thermal processing to simulate recycling, i.e. four cycles of grinding and injection molding, the concentrations of lower brominated BDE were unchanged (Hamm et al. 2001).

A substance must first be absorbed before it can be metabolized systemically. Environmental monitoring demonstrates Deca is uncommonly detected in biological samples (VCCEP 2002), and laboratory studies in both fish and mammals indicate Deca is poorly absorbed. After exposure via water, Deca's bioconcentration factor in fish was <50 (CITI 1992, Hardy 2004). Uptake from food was also extremely low. Over a 120 day period, trout absorbed approximately 0.005% of the 7.5 or 10 mg Deca/kg/d administered in their food (Kierkegaard et al. 1999). Uptake from food by carp at a dose of 940 ng/fish/d was immeasurable; the fish had no detectable Deca after consuming the treated food for 90 days (Stapleton et al. 2004). Nevertheless, Deca's bioavailability in carp was estimated to be 0.4% of the dose based on detection of presumed metabolites. In neither of these studies were the lower brominated diphenyl ethers typically detected in wild fish, BDE-47, 99 and 100, identified as presumed metabolites, and Kierkegaard et al. (1999) concluded that "no evidence of debromination to these congeners was found in this study". Given its low uptake, metabolism of Deca in fish, irrespective of metabolite identity, is an insignificant source of lower brominated diphenyl ethers

Like fish, rats also absorbed Deca to a limited extent from food (0.28-2%) (NTP 1986; El Dareer et al. 1987). Production of metabolites was limited, and likely occurred in the gut rather than systemically. Metabolites were not identified as lower brominated diphenyl ethers. In another study, based on detection of test article-related substances in bile, rats were reported to absorb up to 10% of the Deca administered in formulation specifically designed to enhance uptake (Morck et al. 2003). The primary goal of this study was to determine the identity of Deca metabolites, and thus enhanced uptake was needed in order to maximize conditions for the formation of systemic metabolites (if any). Putative metabolites included three nonabromodiphenyl ethers, which are typical impurities in Deca, and possibly hydroxy derivatives. Brominated diphenyl ethers with less than nine bromine atoms were apparently not formed or present in such small amounts as to be non-detectable. A second study, using samples derived from the previous study as well as from the administration of another formulation designed to enhance absorption, reported similar results with a

maximum uptake of 26% (Sandholm et al. 2003).

Deca is resistant to microbial degradation in sediments, its preferred site of distribution in the environment. Degradation was not observed over a 32-week study with anaerobic freshwater sediment (Schaeffer et al.) or during a two-year study with anaerobic sediment (de Witt 2001). Sediments deposited in Europe over a 20-year period and analyzed for 14 different BDE congeners, including Deca, BDE-47, BDE-99 and BDE-100, had congener patterns characteristic of the Penta mixture (Zegers et al. 2003). This study concluded that the PBDE congener pattern detected in these sediment cores showed a "high resemblance to their pattern in the industrial penta-BDE mixtures" and found no evidence of a contribution from degradation of Deca, which was also detected in these sediments. A more recent attempt to measure the anaerobic degradation rate of Deca in sewage sludge was unsuccessful - Deca's concentration remained unchanged after 114 days. The presence of small amounts of amounts of nona- and octabromodiphenylethers in the sludge indicated that a maximum of 2% of the Deca could possibly have degraded over the 114 days (Gerecke et al. 2004). The tetra and penta PBDEs typically detected in the environment were not found. Actual conversion of Deca to the nona- and octabromodiphenylethers was not detected even after extending the study to 238 days (Kohler et al. 2004).

Environmental monitoring also does not support speculation that Deca degradation is a source of tetra-, penta- and hexaBDEs. Rayne and Ikonomou used pattern analysis in a source reconstruction of PBDEs detected in the Fraser River in British Columbia and concluded that the lower brominated diphenyl ethers detected originated from the Penta and Octa products (Rayne and Ikonomou 2002). They further determined that the most likely source was inefficient rural septic tanks with direct outflows to the river. Song et. al. (2004) concluded that the PBDEs detected in Lake Superior sediment resembled the commercial Penta products and concluded that the PBDEs detected originated from that commercial product. A recent comprehensive analysis of the PBDEs in sludge and effluent from a California wastewater treatment plant indicated that the Penta-mixture was the source of lower brominated diphenylethers detected, not Deca microbial degradation (North et al. 2004). Most recently, Ter Schure et al. (2004) concluded that in environmental samples, "BDE47 and BE99 are markers for the commercial penta-BDE mixture" and that BDE47, BDE100 and BDE99 "originate from the commercial penta-BDE formulations".

Photolytic degradation of Deca to lower brominated diphenyl ethers has been studied by many research groups (Eriksson et al. 2004; Soderstrom et al. 2004; Hua et al. 2003; Barcellos de Rosa et al. 2003; Watanabe et al. 1987). Deca's low aqueous solubility (<0.1 µg/L) has frustrated attempts to directly study its breakdown in that media. Attempts using water/organic solvent mixtures have also been largely unsuccessful. For example, Erikkson et al. (2004) were unable to detect any degradation products of Deca in water, and suggested that Deca's disappearance from the solution may have been due to adsorption to the glass walls of the vessel. As a consequence, most photolysis studies have utilized organic solvents, where Deca has limited solubility. When tested in organic solvents, natural and artificial sunlight cause the small amount of Deca in solution to undergo reductive debromination, ultimately, to diphenyl ether. During this process, lower brominated diphenyl ethers are some of the many substances formed as intermediates, and some of the components of the Penta and OctaBDE commercial products, plus other PBDEs, have been reported on a qualitative basis (Bezarea-Cruz et al. 2004). However, these temporarily formed PBDEs were not those commonly found in environmental samples, and because of this Söderström et. al. concluded that the Penta mixture, and not degradation of Deca, was the most likely

source of the tetra-, penta- and hexaBDEs found in the environment (Soderstrom et al. 2004). In addition, these studies indicate that all of the PBDEs, including BDE-47, 99 and 100, will undergo reductive debromination when in solution in organic solvents, with the rates proportional to the number of bromines on the aromatic rings.

Nevertheless, photolysis studies performed in organic solvents are unlikely to be applicable to Deca's environmental fate. Early in its development as a commercial product, it was recognized, based on other halogenated aromatics, that Deca's photolysis would likely proceed by different routes in water and organic solvents (Norris et al. 1974, 1975). In solvents capable of proton transfer, halogenated aromatics typically degraded by reductive dehalogenation; however, in water, oxidation led to the formation of phenolic compounds. Further, once photohydroxylation was initiated in water, its rate was expected to accelerate as electron-withdrawing halogens were replaced by electron releasing hydroxyl groups. The resulting hydroxylated species were expected to adsorb light more strongly and this ultimately could result in rupture of the aromatic ring. Laboratory findings correlated with the predictions. Only minimal evidence of Deca's (98% purity) aqueous photodegradation was found over a 3-month exposure to natural sunlight, and the degradants were not lower brominated diphenyl oxides. Evidence for degradation of only 0.57% of the amount initially present (10 g/8 l water) was detected after 98 days of exposure to sunlight. However, Deca (7 ppm) in octanol decomposed with a half-life of 4 h. In xylene, a strong absorber of UV light, Deca photodegraded by reductive debromination with a half-life of 15 h on exposure to a 125 watt Hg lamp.

In air, Deca is expected to be associated with particulate matter, rather than in the gaseous phase, because of its low vapor pressure (4.63 x 10-6 Pa) and high adsorption coefficient (1.8 x 106). Deca deposited on dust (silica particles), suspended in dry air, and irradiated with artificial sunlight was found to be photoinert; no measurable degradation to PBDEs occurred (Zetch 2003).

Söderstrom et al. (2004) reported that irradiation of Deca deposited on moist sand, silica gel, sediment or soil resulted in slow formation of unidentified products as well as PBDEs of differing composition from those commonly found in the environment. BDE-47, 99 and 100 were not detected after irradiation of soil, sand or sediment, and these researchers concluded that Deca was not the source of the tetra and pentaBDEs typically detected in the environment. In their concluding paragraph, they said "In this investigation the most commonly found PBDEs in environmental samples (BDE 47, BDE 99 and BDE 100) were only formed to a minor degree from the photolysis of DecaBDE and only in toluene and/or on silica gel. BDE 153 was formed in toluene, on sand outdoors and on sediment. The origin of these congeners in the environment is probably primarily from emission of technical PentaBDE products and possibly from other degradation pathways of DecaBDE. To further investigate the degradation pathways of decaBDE, combined photolytic/bacterial degradation pathways should be examined."

The weight of the evidence from degradation (thermal, microbial, metabolic, photolytic) and monitoring studies is consistent with the conclusion that the tetra, penta, hexa and hepta PBDEs found in environment are not the result of Deca reductive debromination, but rather from dispersal of the Penta mixture. Prevedourus et al. (2004) reached a similar conclusion.

Reliability : (1) valid without restriction
16.08.2005 (32) (33) (96) (97) (98) (34) (99) (100) (101) (35) (102) (94) (103) (104) (83) (37) (105) (10) (106) (107) (108) (109) (110) (93) (38) (111) (112) (39) (113) (114) (40)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
LC50	:	> 500 measured/nominal
Limit test	:	yes
Analytical monitoring	:	
Method	:	other
Year	:	1992
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	48 Hour LC50 Study

A 48-hour LC50 for orange-red killifish (Oryzias latipes) was determined for DBDPO as part of a six-week bioconcentration study. The LC50 was >500 mg/l (CITI 1992).

Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

03.08.2005 (96)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	
Endpoint	:	other: growth
Exposure period	:	
Unit	:	mg/l
EC50	:	> 1 measured/nominal
Limit test	:	yes
Analytical monitoring	:	yes
Method	:	other
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	EC50 in 3 Species of Marine Algae

Walsh et al. (1987) studied the toxicity of DBDPO to the marine unicellular algae Skeletonema costatum, Thalassiosira pseudonana and Chlorella sp. The tests were carried out at a salinity of 30o/oo for either 72 hours (S. costatum and T. pseudonana) or 96 hours (Chlorella sp.). The end-point measured was the EC50 for growth based on cell numbers. The exposure concentrations in the test solutions were verified by analysis.

In the tests, the DBDPO was added as a solution in acetone (final acetone concentration around 1 ml/l). Six different growth media were used in the test, one natural seawater and five synthetic seawater formulations. The natural seawater had a salinity of 32‰ and was diluted to give a final test salinity of 30‰ to be comparable with that of the synthetic media. The pHs of the various test media were in the range 7.6?8.2.

The EC50 for all three species was greater than the highest concentration

tested (1 mg/l), and was substantially greater than DBDPO's water solubility.

03.08.2005 (115)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	other:sewage sludge organisms
Species	:	activated sludge of a predominantly domestic sewage
Exposure period	:	3 hour(s)
Unit	:	mg/l
NOEC	:	>= 15 measured/nominal
Method	:	OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	Activated Sludge Respiration Inhibition Test

An activated sludge respiration inhibition (OECD 209) test was performed on a composite sample of commercial DBDPO products from three manufacturers (Schaefer and Siddiqui, 2001). The purity of the test substance was 97.9% DBDPO. The substance was tested in triplicate at a concentration of 15 mg/l. The inoculum used in the test was activated sludge from a waste water treatment plant that received predominantly domestic waste. The test was carried out at 20-22oC and the respiration rate of the activated sludge over 3 hours was determined. Two controls and a positive control (3,5-dichlorophenol at concentrations of 5, 15 and 50 mg/l) were also run. The respiration rates in the two controls were both 41.6 mg O2/l/hour. The mean respiration rate in the DBDPO treatments was 41.1 mg O2/l/hour and so no inhibition of respiration was seen at the concentration tested. The EC50 for the positive control was determined as 9.8 mg/l, which was within the normal range of 5 to 30 mg/l for this test. The NOEC for DBDPO from this test was therefore >15 mg/l. This indicates DBDPO's lack of ready biodegradation is not due to inhibition of the microorganisms present in sewage sludge.

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (116)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Attached document	:	DBDPO is not expected to be chronically toxic to aquatic organisms owing to its lack of acute toxicity, negligible water solubility, and tests on the commercial OBDPO product. A long-term Daphnia test has been performed on the commercial OBDPO product, and no effects on survival, reproduction or growth were seen over 21-days at concentrations up to 2 µg/l (solubility limit). Taken as a whole, it is clear that the aquatic toxicity and bioaccumulation potential of the PBDPO products (penta?, octa? and decabromodiphenyl oxide) decreases with increasing bromination and therefore it is unlikely that DBDPO will show any toxic effects to invertebrates at concentrations below its solubility limit.

02.08.2005

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

Species	:	Lumbriculus
Endpoint	:	other: survival/reproduction, growth
Exposure period	:	28 other: days
Unit	:	mg/kg sediment dw
NOEC	:	>= 5000 measured/nominal
Method	:	ASTM E1706-95b sediment toxicity test
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Two 28-Day Sediment Organism Toxicity Studies (2.5 and 5% TOC)

Prolonged sediment toxicity tests (28-D) on DBDPO were preformed with the oligochaete Lumbriculus variegatus using a flow-through test system with sediments of either 2.4% or 5.9% organic carbon content (Krueger et al. 2001a,b). The test was based on the ASTM E 1706-95b Guideline and USEPA Series 850 Ecological Effects Test Guidelines (OPPTS No. 850.1736) and performed according to Good Laboratory Practices.

The test substance was a composite sample from three manufacturers and had a purity of 97.9%. The total exposure period was 28 days. The nominal concentrations tested in the studies were 0, 313, 625, 1,250, 2,500 and 5,000 mg/kg dry weight. Each treatment and control group was replicated eight times with ten oligochaetes/replicate. Additional replicates were also run in each treatment and control group for analytical sampling of water and sediment. The endpoints were survival/reproduction (as measured by the total number of organisms present which is a combination of parent survival and reproduction) and growth (as determined by dry weight of organism).

In both the 2.4 and 5.9% organic carbon sediment, the NOEC for survival and growth >= 5,000 mg/kg dry sediment (nominal). Based on the measured sediment concentrations, the NOECs were 4,536 and 3,841 mg/kg dry weight for the 2.4 and 5.9% organic carbon sediments, respectively.

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (117) (118)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	other terrestrial plant: corn, cucumber, ryegrass, onion, soybean, tomato
Endpoint	:	other: emergence, growth
Exposure period	:	21 day(s)
Unit	:	mg/kg soil dw
NOEC	:	>= 5347 measured/nominal
Method	:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Effect on Seedling Emergence and Growth in Six Terrestrial Plant Species

The potential effects of DBDPO on seedling emergence and growth over a 21 day period were tested in six species of terrestrial plants: Corn (Zea mays), Cucumber (Cucumis sativa), Onion (allium cepa), Ryegrass (Lolium perenne), Soybean (Glycine max), Tomato (Lycopersicon esulentum). The

study was performed according to the proposed revision of OEFCD Guideline 208, OPPTS 850.4100 (Public Draft), OPPTS 850.4225 (Public Draft) and Good Laboratory Practices. The test article was a composite of the commercial products produced by Albemarle Corporation, Great Lakes Chemical Corporation, and Dead Sea Bromine Group.

The test consisted of a negative control and 5 treatment groups. Each group had 4 replicate pots with ten seeds planted in each pot. Test concentrations of DBPDO were made by soil incorporation to each treatment group prior to planting of seeds. The nominal test concentrations were 0, 391, 781, 1563, 3125 and 6250 mg/kg dry soil. Mean measured concentrations were <LOQ, 292, 707, 1177, 2098 and 5349 mg/kg dry soil. Observations of emergence and general assessments of seedling condition were made on Days 7, 14 and 21, while observations of height, shoot dry weight, an dassignment of plant condition scores were made only on Day 21.

The soil incorpoation of DBDPO caused no effects on emergence, surival or growth on any of the six plant species tested. The highest soil concentration tested, 6250 mg/kg dry soil (nominal) or 5349 mg/kg dry soil (measured), was the NOEC for all six species. (Porch and Krueger 2001).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (51)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type	:	artificial soil
Species	:	Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint	:	other:survival, reproduction
Exposure period	:	56 day(s)
Unit	:	mg/kg soil dw
NOEC	:	= 4910 measured/nominal
LC50	:	> 4910 measured/nominal
Method	:	EPA OPPTS 850.62
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Earthworm Survival and Reproduction

The effect of DBDPO on the survival and reproduction of the earthworm, Eisenia fetida, was investigated in a 56-day test using artificial soil. The study was performed according to US EPA OPPTS Guidline 850.620, OECD Guideline 207, OECD proposed guideline for Earthworm Reproduction Test, and Good Laboratory Practices. The test article was a composite of the commercial products produced by Albemarle Corporation, Great Lakes Chemical Corporation, and Dead Sea Bromine Group.

The primary objective of the study was to estimate the chronic toxicity of DBDPO by determining the ten (EC10) and fifty (EC50) percent effect concentrations for adult worm survival and reproductive output during the course of the test. Nominal test concentrations were 0, 312.6, 650, 1250, 2500 and 5000 mg/kg of dry soil. Mean measured test concentrations were <100, 320, 668, 1240, 2480 and 4910 mg/kg of dry soil. After 28 days of exposure, worms were composited by treatment and placed in glass dishes containing wet paper towels to allow the worms to adequately purge their gut contents. After 48 hours, the worms were transferred to sample vials and stored frozen until analysis for DBDPO tissue concentrations. Analysis of both soil concentrations and worm tissue

concentrations consisted of extraction with THF followed HPLC/UV. The artificial soil was characterized as a sandy loam (International Textural Class; Hydrometer method) composed of 69% sand, 18% silt and 13% clay. The percent organic matter (Carbon) was 8.0 (4.7). The disturbed bulk density was 0.78 gm/cc, and the cation exchange capacity was 10.3 (meq./100 g). Adult worms were used, ranging in weight from 347.4 to 587.3 mg wt weight at test initiation.

The 28-day EC10 and EC50 for survival were > 4910 mg/kg dry soil. The 56-day EC10 and EC50 for reproduction were > 4910 mg/kg dry soil. The NOEC for survival and reproduction was 4910 mg/kg dry soil, the highest dose tested. Measured concentrations of DBDPO in the worm tissue samples, regardless of treatment level, were below the limit of quantification (LOQ=0.750 ug/g). Thus, DBDPO did not bioaccumulate in the earthworms. (Aufterheide et al. 2001).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (45)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

Type : other: earthworm
Deg. product :

Attached document : Earthworm Survival and Reproduction Study: Measured Concentrations in Earthworm Tissues

Measured concentrations of DBDPO in the worm tissue samples after 28 days of exposure, regardless of treatment level, were below the limit of quantification (LOQ=0.750 ug/g). Thus, DBDPO did not bioaccumulate in the earthworms (Aufterheide et al. 2001).

See Section 4.6.1 for details on this study.

Reliability : (1) valid without restriction
03.08.2005 (45)

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Attached document : Discussion of ADME Studies

The uptake, distribution and elimination of DBDPO after oral or intravenous (IV) dosing in the rat have been evaluated in several studies (NTP 1986; Norris et al. 1973, 1974; El Dareer et al. 1987; Morck and Klassen-Wheler 2001; Morck et al. 2003; Sandholm et al. 2004). These processes were monitored by following total 14C-radioactivity after administration of labeled-DBDPO or by following total bromine content via neutron activation after administration of DBDPO. NTP evaluated the uptake and disposition of DBDPO in the rat as part of the two-year bioassay. Four studies were performed and the results were reported in the 1986 NTP report (NTP, 1986) and in the publication of El Dareer et al. (1987). Earlier studies are reported in Norris et al. (1974, 1975). Similar work was performed more recently by Morck et al. (2003) and Sandholm et al. (2004).

In the dietary NTP-sponsored studies conducted by El Dareer et al. (1987; NTP 1986), DBDPO treatment for 7 days at varying dose levels preceded treatment with the radiolabeled compound. Pretreatment dose levels were 51,000, 25,400, 4,730,2,510, 496 and 238 ppm in the diet. Test articles used for pretreatment in the 14C-DBDPO studies (NTP 1986; El Dareer et al. 1987) closely resembled today's commercial product which is >= 97% DBDPO. In the studies conducted by Norris et al. (1973; 1975), a single dose of 14C-DBDPO was administered orally or bromine tissue levels were monitored by neutron activation after repeated administration of DBDPO for 3, 6 or 12 months. The test article for the neutron activation experiments was the former low purity product "Dow FR-300-BA" composed of 77.4% DBDPO, 21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide. In the Morck and Kassen Wheeler (2001) study, 14C-DBDPO was synthesized in the laboratory.

The NTP studies by El Dareer et al. (NTP 1986; El Dareer et al. 1987) showed that DBDPO was poorly absorbed (2-0.28% of the oral dose) from the gastrointestinal tract at all pretreatment doses (277-50,000 ppm in the diet, respectively) and rapidly eliminated. The whole body half-life was < 24 hr. Excretion in the urine accounted for ~0.01% of the dose. Feces was the major route of elimination. Greater than 99% of the dose was recovered in the feces by 72 hr post-dosing. At all oral doses tested (277 - 50,000 ppm in the diet), the majority of the test article (~98 - 70%, respectively) was eliminated as the parent molecule. Three metabolites were detected in the feces and ranged from ~2 to 30%, respectively, of the total recovered 14C-label. The highest percentage of metabolites (~30% of the dose) was present in the feces of animals pretreated with higher doses of DBDPO (25,000 and 50,000 ppm) in the diet. The lowest percentage of metabolites (~2% of the dose) was present in the feces of animals pretreated with lower levels of DBDPO (277 ppm). The identity of the metabolites was not determined.

Only trace levels of the 14C-label were detected in any organ or tissue at any time point (24, 48 or 72 hr post dosing with the radiolabel) (NTP 1986; El Dareer et al. 1987). The maximum total 14C-activity detected in the body at any time was only ~1% of the oral dose. The maximum 14C-activity, calculated as the sum of the radioactivity in liver, kidneys, lungs, spleen, brain, muscle, skin, fat, and blood, was detected in the 277 ppm treatment group 24 hr post-dosing. Studies utilizing intravenous (IV) administration of 1 mg 14C-DBDPO/kg and bile duct canulation showed that the 14C-label was excreted in the bile as the parent molecule and 3 metabolites.

Approximately 60% of the dose was eliminated as metabolites after IV administration. The bile contained 7.17% of the IV dose within 4 hr post-doing, and 2.2% of the dose was excreted in the bile per hr.

The above results are consistent with earlier reports by Norris et al. (1973, 1975). Norris et al. (1975) administered 1 mg/kg 14C-DBDPO orally to 3 male and 3 female rats. The level of radioactivity found in the expired air and urine, measured at 24 hr intervals over a 16-day period, was < 1 %. The principal route of excretion was the feces. The rate of excretion was the same for both sexes. Within the first 24 hr post-dosing, 90.6% of the administered dose was detected in the feces, and 99% of the 14C-activity was accounted for by day 2. Tissues (adipose, heart, skin, adrenals, spleen, liver, pancreas) taken on day 16 post-dosing showed no 14C-label with the exception of the adrenal (0.01% of the dose) and spleen (0.06% of the dose). The 14C-activity in these two tissues was at the limit of detection. The half-life of the disappearance of 14C-activity from the body of DBDPO-treated rats was < 24 hours.

Norris et al. (1973, 1975) also measured bromine concentrations (via neutron activation analysis) in the kidney, skeletal muscle, serum testes, liver and adipose tissue in male and female rats maintained on diets providing 1, 0.1, 0.01 and 0 mg DBDPO mixture/kg/day for 6 or 12 months. The composition of the DBDPO mixture (Dow FR-300-BA) was 77.4% DBDPO, 21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide. After 180 days of treatment, mean bromine levels in the control and treatment groups in liver, kidney, skeletal muscle, serum and testes were statistically comparable. The mean bromine level in adipose tissue from the 0.1 mg/kg/day dose group (~3.3 ug/g) was statistically greater than the control mean (~1.7 ug/g). After 12 months on treatment, bromine concentrations in both the liver and adipose tissue were statistically comparable to controls.

Norris et al. (1975) evaluated the elimination of bromine from liver and adipose tissue. Male rats were maintained for 90 days on diets providing a dose of 1 mg DBDPO mixture (Dow FR-300-BA)/kg/day and then placed on control diet. Kidney, serum, adipose tissue, and liver were analyzed for bromine by neutron activation analysis. On recovery day 0 there was no difference in bromine content in kidney or serum between the control and treated rats. After 10 days on the control diet, bromine concentrations in the liver of treated rats were comparable to controls. Adipose bromine levels in the treated group (~2.5 - 4 ug/g) were higher than the controls (~0 - 2 ug/g) during the recovery period.

Morck and Klassen Wehler (2001) reported similar results. Male rats were gavaged with a single dose of 14C-DBDPO (3 umol/kg; 0.00288 ug/kg). Feces were the predominant excretory route and contained ~90% of the dose within 3 days. Only trace amounts were eliminated in the urine (<0.5% of the dose). Approximately 9.5% of the dose was recovered in the bile within 3 days, and this figure was reported as the percent of dose absorbed. Approximately 3% of the dose remained in tissues at 72 hr post-dosing. The majority of the 14C-activity was detected in the liver followed in declining amount in the muscle, skin, adipose tissue and colon wall plus contents. Eight phenolic metabolites were reported in the feces, and included di-substituted penta- to octaBDPOs. Trace amounts of 3 nona-BDDPOs were also reported.

A full publication of the Morck and Klassen Wehler abstract was published in 2003. That publication provides details not available in the abstract. These details are important, because this study has been cited as demonstrating that DBDPO's absorption was higher than earlier reported. Morck et al. (2003) reported their study utilized a test article/vehicle formulation specifically designed to enhance absorption in order to study

possible metabolites: "To improve absorption when compared with previous studies of decaBDE, emphasis was placed on formulation of the dose in a novel vehicle to enhance decaBDE solubility, without exceeding the level used for tetraBDE and pentaBDE studies."

The paper concluded that the higher absorption noted in this study was likely due to the formulation, i.e. soya phospolipone/Lutrol/water. Lutrol is used in the pharmaceutical industry to enhance the solubility and bioavailability of poorly water-soluble drugs. Lutrol 127 is a pluronic block copolymer. These copolymers incorporate drugs into micelles to increase solubility (Kabanov et al. 2003; Kabonov and Alakhov 2002), and are used to enhance oral and brain bioavailability of drugs. Pluronic copolymers also inhibit drug efflux transporters, e.g. P-glycoprotein. P-glycoprotein is part of an active transport elimination (not absorption as stated by Morck and Klassen Wehler) mechanism in the intestine (Charman 2000; Tsuji and Tamai 1996). The P-glycoprotein system is actually an absorption barrier. The net result of this formulation was with respect to DBDPO was increased solubility, enhanced absorption, and prolonged circulation time.

Morck and Klassen Wehler (2001) and Morck et al. (2003) based their absorption estimate on the amount of radiolabelled compound in bile; e.g. their assumption of 9.5% DBDPO absorption was based on the proportion of the 14C-activity administered that was detected in the bile (8.4%). The 14C-activity in bile was largely in the form of metabolites, rather than parent molecule, and absorption is traditionaly based on the parent molecule. By using this approach, the Morck papers failed to account for pre-systemic metabolism in the gut since the total 14C-activity in the bile was used to estimate percent absorption. When estimating systemic or absolute bioavailability, the parent molecule and metabolites should be differentiated (Gibaldi and Perrier 1982). Thus, Morck et al.'s absorption estimate for DBDPO was artificially increased.

Morck et al. also assumed that debromination of DBDPO was responsible for the trace amounts of nonaBDEs detected. However, the test article was only 98% pure and nonaBDE's are known to be a major impurity in DBDPO. Thus, the nonaBDEs detected could have been those present in the test article rather than actual metabolites.

Sandholm et al. represents research conducted in Ms. Sandholm's pursuit of her graduate degree. Plasma samples derived from the Morck et al. (2003) study that utilized the Lutrol formulation were analyzed, and a separate pharmacokinetic study in rats using non-radiolabelled DBDPO was performed. In the pharmacokinetic study, Sandholm et al. utilized PEG 400 in the dosing formulation and quantitated plasma levels of DBDPO and metabolites with GC/MS (SIM) and GC/MS (ECNI), respectively. Like Lutrol, PEG 400 is used in the pharmaceutical industry to enhance uptake of drugs. It is widely used to enhance solubilization of both intravenous and oral studies during drug discovery (Joshi et al. 2004; Temesi et al. 2003), and has been shown to inhibit P-glycoprotein and cytochrome P450 activity in intestinal cells in vitro (Johnson et al. 2002).

Sandholm et al. reported that her pharmacokinetic study indicated an oral bioavailability, defined as that fraction of the dose to reach the systemic circulation, of 26%. This is substantially higher than that reported by NTP, El Dareer et al. or Morck et al (2003). PEG 400 appears to have a greater ability to enhance DBDPO's availability than Lutrol.

Sandholm et al. reported DBDPO was the major compound detected in blood. Only trace levels (< 0.5% of DBDPO's level) of 3 nonaBDEs were detected. These nonaBDEs could have originated from the test article, rather than from debromination of DBPDO in vivo. Two phenolic metabolites were also reported, e.g. monohydroxylated octa- and

nonaBDE, but their amounts relative to DBDPO were not. Both nona- and OctaBDE congeners are potential impurities in the test article, and hydroxylation of the phenyl ring would be an expected route of metabolism. A third metabolite, purportedly a methyl derivative of a guaiacol-type structure, was also reported, but its relative amount was not. Neither Morck nor Sandholm et al. considered that enhanced solubilization, due to the unique formulations, may have enhanced the availability of DBDPO to gut bacteria.

With the exception of reporting a higher oral bioavailability, Sandholm's paper provides essentially no new information with respect to DBDPO. She confirms that DBDPO was rapidly eliminated, had a low volume of distribution, and was not preferentially distributed to adipose tissue. She confirms that the parent molecule, DBPDO, was the predominant molecule in plasma and that the dominant metabolites were monohydroxy octa/nonaBDEs - both of which could have been produced from impurities in the test article. Her failure to detect numerous and/or a high proportion of metabolites in plasma argues against extensive metabolism. Her work does not confirm that DBDPO was debrominated in vivo or that any metabolism took place in the liver as opposed to the intestinal cell or gut bacteria. Her work does not confirm DBDPO is extensively metabolized as she relied on Morck's work for this interpretation, and the results of her own pharmacokinetic study dispute this. Finally, she alleges that retention of phenolic metabolites or possible generation of lower brominated diphenyl ethers (reported in vitro by Meerts et al. 2000) could be a risk. In saying this, she fails to take into consideration the large toxicological database on DBDPO that indicates a no-adverse-effect-level of at least 1000 mg/kg/d. Finally, Lutrol or PEG in the dosing formulations can be expected to have enhanced DBDPO's bioavailabity and prolonged its elimination.

Based on the findings of NTP, El Dareer et al. and Norris et al. (NTP 1986; Norris et al. 1973, 1975; El Dareer et al. 1987), DBDPO is poorly absorbed from the gastrointestinal tract as would be expected for a molecule of this size, weight and poor solubility. Following oral administration of 14C-DBDPO, only trace levels of radioactivity were found in organs/tissues at any time point. The parent molecule (and all metabolites) was rapidly eliminated - > 99% of the dose was recovered in the feces and gut contents within 72 hours of oral dosing. The overwhelming route and form of elimination was by fecal excretion as the parent molecule. Less than 0.01% of the oral dose was excreted in the urine. DBDPO was capable of being metabolized; the parent molecule and 3 metabolites were detected in feces following oral or IV dosing of rats. The lower the dietary dose the lower the percent eliminated as metabolites, e.g. at a pretreatment dose of 277 ppm in the feed, approximately 2% of the dose was eliminated as metabolites. Recent studies by Morck and Klassen Wheeler (2001), Morck et al. (2003) and Sandholm et al. (2003) reported similar findings to that of NTP and El Dareer.

Reliability : (1) valid without restriction
16.08.2005 (98) (119) (120) (83) (121) (10) (108)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	female
Number of animals	:	
Vehicle	:	other: corn oil
Doses	:	126, 252, 500, 1,000 or 2,000 mg/kg

Method	:	other
Year	:	1973
GLP	:	no data
Test substance	:	other TS: FR BA300 (77.4% DBDPO, 21.8% NonaBDPO and 0.8% OBDPO)
Attached document	:	Intragastric intubation of a single dose of a 10% corn oil suspension of DBDPO (Dow FR 300 BA: 77.4% DBDPO, 21.8% NonaBDPO and 0.8% OBDPO) to female Sprague Dawley rats resulted in the survival of all rats at doses of 126, 252, 500, 1,000 or 2,000 mg/kg. No indication of toxicity after intubation or during the 14-day period was observed. No gross pathological changes were observed at necropsy carried out on one rat/dose level (Norris et al., 1973).
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (31)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC0
Value	:	> 48.2 mg/l
Species	:	rat
Strain	:	other: Spartan
Sex	:	male/female
Number of animals	:	
Vehicle	:	
Doses	:	2 or 48.2 mg/L
Exposure time	:	1 hour(s)
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	Groups of 5 male and 5 female Spartan rats were exposed for one hour to 2 or 48.2 mg/l DBDPO (DE-83) in air and subsequently observed for 14 days. All rats survived. Dyspnea and ocular discharge were noted from 2 mg/l concentration (one animal); moreover, in the 48.2 mg/l group, eye squint and increasing motor activity were observed. All rats were normal at the end of 14-day observation period. Necropsies were not performed (Great Lakes 1974c).
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

16.08.2005 (122)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	
Vehicle	:	no data
Doses	:	200 or 2000 mg/kg bw
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document	:	Groups of 2 male and 2 female New Zealand White rabbits were administered single doses of 200 or 2,000 mg/kg of DBDPO (DE-83) applied neat under occlusive wraps for 24 hours: all the animals survived. Animals were observed for 14 days. At the 2,000 mg/kg dosage level all rabbits exhibited normal body weight gains. Local and general signs of toxicity were not reported and necropsies not performed (Great Lakes 1974b).
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

16.08.2005 (123)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	100 %
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	
Vehicle	:	other: no vehicle was used
PDII	:	0
Result	:	not irritating
Classification	:	not irritating
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO as dry solid (500 mg), cause no irritation on intact or abraded skin when applied to shaved skin under occlusion to 2 groups of 3 New Zealand White rabbits. No erythema or edema was observed after a single exposure for 24h and followed by an observation period of 72h (Great Lakes 1974d).
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

01.08.2005 (124)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other
Year	:	1973
GLP	:	no data
Test substance	:	other TS: 77% DBDPO
Attached document	:	Norris et al. (1973 and 1974) reported that DBDPO applied as dry solid on shaved skin of New Zealand albino rabbits caused essentially no response on intact skin and a slight erythematous and edematous response on abraded skin after a single confined exposure of 24 hours. Repeated exposures to intact skin for five days/week for two weeks and to abraded

skin for three days did not alter the responses observed following a single administration.

Reliability : (2) valid with restrictions
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (31) (83)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration :
Dose : 100 other: mg
Exposure time : unspecified
Comment :
Number of animals :
Vehicle : other: none
Result : not irritating
Classification : not irritating
Method : other
Year : 1974
GLP : no data
Test substance :

Attached document : Studies with 3 male and 3 female New Zealand White rabbits showed that 100 mg DBDPO (93 - 98.5% purity) as dry solid caused transient (reversible in 48h) mild irritation of the conjunctival membranes. The cornea, iris and lens were unaffected (Great Lakes 1974e).

Reliability : (2) valid with restrictions
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (125)

5.3 SENSITIZATION

Type : Patch-Test
Species : other: human
Number of animals :
Vehicle :
Result : not sensitizing
Classification : not sensitizing
Method : other
Year : 1974
GLP : no data
Test substance :

Attached document : Human Patch Tests for Skin Sensitization

In 50 human subjects, repeated application of a suspension of 5% DBDPO in petrolatum 3 times a week for 3 weeks and challenged two weeks subsequent to the last induction application did not result in skin sensitisation. Skin irritation was observed in 9 out of the 50 persons (Norris et al. 1974; WHO 1994).

Human volunteers (80 males and 120 females) were treated with 9 induction patches of 2 batches of DBDPO. The first sample was evaluated as received, and the second as a 2% (w/v) aqueous solution. The patches were applied once every 2 days, allowed to contact the skin for 24h, and the skin was graded for irritation. Fifteen (15) subjects among the 200 volunteers showed some slight irritation reactions: very slight erythema - barely perceptible in 14/1,800 patches and mild - well defined erythema in

2/1,800 patches and very slight edema - barely perceptible in 1/1,800 patches. After a non-patching period of 12 days, the challenge patch was applied to detect sensitisation. No evidence of skin sensitisation with either of the test materials in any of the subjects tested was observed (Industrial Bio-Test Laboratories, 1975).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (126) (121) (11)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	14 days
Frequency of treatm.	:	continually in the diet
Post exposure period	:	
Doses	:	5,000, 10,000, 20,000, 50,000 or 100,000 ppm DBDPO in the diet
Control group	:	yes, concurrent no treatment
NOEL	:	>= 100000 ppm
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : U.S. NTP 14-Day Repeated Dose Studies in Rats and Mice (1986)

DBDPO administered at 10% of the diet for 14 days produced no adverse effects in F344/N rats and B6C3F1 mice (NTP 1986).

Groups of five males and five females were fed diets containing 0, 5,000, 10,000, 20,000, 50,000 or 100,000 ppm DBDPO for 14 days. Male and female F344/N rats and B6C3F1 mice were obtained from Charles River Breeding Laboratories and held for approximately 3 weeks before the studies began. Animals were assigned to groups such that cage weights were approximately equal at initiation of the study. Animals were housed 5 per cage (polycarbonate) on heat-treated hardwood chips. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration.

Rats and mice were observed daily for clinical signs of toxicity and were weighed on days 1, 7 and 14. A necropsy was performed on all animals in all doses. Organs examined at the gross necropsy included gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, thigh muscle, sciatic nerve, sternebrae, femur or vetebrae including marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, tissue masses, ileum, colon, cecum, rectum, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary gland, spinal cord and eyes.

DBDPO doses up to 10% (100,000 ppm) of the diet in F344/N rats and B6C3F1 mice produced no mortality, no effect on body weight, and no compound-related clinical signs or gross pathologic effects (histopathology was not performed). The test article in the 14 day study was 99% pure DBDPO.

Reliability : (1) valid without restriction

Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Sub-chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : oral feed
Exposure period : 14 days
Frequency of treatm. : continually in the diet
Post exposure period :
Doses : 5,000, 10,000, 20,000, 50,000 or 100,000 ppm
Control group : yes, concurrent no treatment
NOEL : >= 100000 ppm
Method : other
Year : 1986
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : U.S. NTP 14-Day Repeated Dose Studies in Rats and Mice (1986)

DBDPO administered at 10% for 14 days produced no adverse effects in F344/N rats and B6C3F1 mice (NTP 1986).

Groups of five males and five females were fed diets containing 0, 5,000, 10,000, 20,000, 50,000 or 100,000 ppm DBDPO for 14 days. Male and female F344/N rats and B6C3F1 mice were obtained from Charles River Breeding Laboratories and held for approximately 3 weeks before the studies began. Animals were assigned to groups such that cage weights were approximately equal at initiation of the study. Animals were housed 5 per cage (polycarbonate) on heat-treated hardwood chips. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration.

Rats and mice were observed daily for clinical signs of toxicity and were weighed on days 1, 7 and 14. A necropsy was performed on all animals in all doses. Organs examined at the gross necropsy included gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, thigh muscle, sciatic nerve, sternebrae, femur or vetebrae including marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, tissue masses, ileum, colon, cecum, rectum, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary gland, spinal cord and eyes.

DBDPO doses up to 10% (100,000 ppm) of the diet in F344/N rats and B6C3F1 mice produced no mortality, no effect on body weight, and no compound-related clinical signs or gross pathologic effects (histopathology was not performed). The test article in the 14 day study was 99% pure DBDPO.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 90 days
Frequency of treatm. : continually in the diet

Post exposure period	:	no
Doses	:	3, 100, 6,200, 12,500, 25,000 or 50,000 ppm
Control group	:	yes, concurrent no treatment
NOEL	:	>= 50000 ppm
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : U.S. NTP 13-Week Repeated Dose Studies in Rats and Mice (1986)

In the 13-week study, DBDPO doses up to 5% of the diet in F344/N rats (n = 10 rats/sex/dose) and B6C3F1 mice (n = 10 mice/sex/dose) produced no mortality, no effect on body weight, and no compound related gross or microscopic pathologic effects. The dietary dose levels were 0, 3, 100, 6,200, 12,500, 25,000 or 50,000 ppm DBDPO and were fed for 13 weeks.

Four-week-old male and female F344/N rats and 5-wek-old B6C3F1 mice were obtained from Charles River Breeding Laboratories, observed for 4 weeks, and assigned to cages according to a table of random numbers. The cages were then assigned to dosed and control groups according to another set of random numbers. Animals were housed five per cage (polycarbonate) on heat-treated hardwood chips. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration. Animals were checked twice daily; moribund animals were sacrificed. Feed consumption was measured weekly by cage. Animal weights were recorded weekly. Clinical signs and behavior was recorded weekly. At the end of the 13-week studies, survivors were sacrificed and a necropsy was performed on all animals. Approximately 30 tissues were examined histologically in the control and high dose groups: gross lesions and tissue masses, mandibular or mesenteric lymph nodes, salivary gland, sternebrae, femur or vertebrae including marrow, thyroid, parathyroids, small intestine, colon, liver, gallbladder (mice), prostate/testes or ovaries/uterus, lung and mainstem bronchi, heart, esophagus, stomach, brain, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, pituitary gland, spinal cord (if neurologic signs present), eyes if grossly abnormal), and mammary gland. The test article used in this study consisted of two lots of DBDPO; one lot was that used in the 14 day study and the second was ~97% pure DBDPO.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
29.07.2005 (127)

Type	:	Sub-chronic
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatm.	:	continually in the diet
Post exposure period	:	no
Doses	:	3, 100, 6,200, 12,500, 25,000 or 50,000 ppm
Control group	:	yes, concurrent no treatment
NOEL	:	>= 50000 ppm
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : U.S. NTP 13-Week Repeated Dose Studies in Rats and Mice (1986)

In the 13-week study, DBDPO doses up to 5% of the diet in F344/N rats (n = 10 rats/sex/dose) and B6C3F1 mice (n = 10 mice/sex/dose) produced no mortality, no effect on body weight, and no compound related gross or microscopic pathologic effects. The dietary dose levels were 0, 3, 100, 6,200, 12,500, 25,000 or 50,000 ppm DBDPO and were fed for 13 weeks.

Four-week-old male and female F344/N rats and 5-wek-old B6C3F1 mice were obtained from Charles River Breeding Laboratories, observed for 4 weeks, and assigned to cages according to a table of random numbers. The cages were then assigned to dosed and control groups according to another set of random numbers. Animals were housed five per cage (polycarbonate) on heat-treated hardwood chips. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration. Animals were checked twice daily; moribund animals were sacrificed. Feed consumption was measured weekly by cage. Animal weights were recorded weekly. Clinical signs and behavior was recorded weekly. At the end of the 13-week studies, survivors were sacrificed and a necropsy was performed on all animals. Approximately 30 tissues were examined histologically in the control and high dose groups: gross lesions and tissue masses, mandibular or mesenteric lymph nodes, salivary gland, sternebrae, femur or vertebrae including marrow, thyroid, parathyroids, small intestine, colon, liver, gallbladder (mice), prostate/testes or ovaries/uterus, lung and mainstem bronchi, heart, esophagus, stomach, brain, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, pituitary gland, spinal cord (if neurologic signs present), eyes if grossly abnormal), and mammary gland. The test article used in this study consisted of two lots of DBDPO; one lot was that used in the 14 day study and the second was ~97% pure DBDPO.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
29.07.2005 (127)

Type : Chronic
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : two years
Frequency of treatm. : continually in the diet
Post exposure period : no
Doses : 2.5 or 5% in the diet
Control group : yes, concurrent no treatment
Method : other
Year : 1986
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : U.S. NTP Two Year Studies in Rats and Mice (1986)

Doses of 2.5 or 5% DBDPO in the diet for two years (103 weeks) were well tolerated by F344/N rats (n=50 rats/sex/dose) and B6C3F1 mice (n=50 mice/sex/dose) with no effect on body weight or mortality and only minimal evidence of organ effects (NTP 1986). The U.S. National Toxicology Program (NTP) estimated the average amount of DBDPO consumed per day in the two year study to be 1,120 mg/kg and 2,240 mg/kg for low and high dose male rats, respectively, and 1,200 mg/kg and 2,550 mg/kg for low and high dose female rats, respectively. Likewise, NTP estimated the average DPDPO consumed per day by mice in the two year study was 3,200 and 6,650 mg/kg for low and high dose male mice, respectively, and 3,760 and 7,780 mg/kg for low and high dose female mice, respectively. The test article used in this study consisted of two lots of DBDPO that were

96% or 94-97% pure DBDPO, respectively.

Animals used in the 2-year study were produced under strict barrier conditions at Charles River Breeding Laboratories. Animals were shipped to the test laboratory at 5-6 weeks of age, quarantined for 14 (rats) or 16 (mice) days, and placed on the study when 7-8 (rats) and 9 (mice) weeks old. Animals were housed in polycarbonate cages with heat-treated hardwood chips. Rats and female mice were housed 5/cage, male mice 5/cage until month 8 and then 1/cage for intermittent periods, and 1/cage after 15 months. The animal room environment was 68-80 degrees F, 15-90% humidity, fluorescent lighting 12 hours/d, and with 10-12 room air changes/hour. Animals were randomized to groups by weight class and then to dose groups. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration.

Animals were observed twice per day, weighed initially and then once/week for 12 weeks and monthly thereafter until wk 100 or 101 when observations were performed every 2 weeks. All animals were subjected to a necropsy and histologic examination of tissues. The tissues examined histologically were gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, sternum (including bone marrow), thymus, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, pancreas, gallbladder (mice), small intestine, colon, mesenteric lymph nodes, liver, spleen, kidneys, adrenal glands, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary gland, tissue masses, and regional lymph nodes. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Organ effects reported in high dose male rats (~2,240 mg/kg/d) at the conclusion of NTP's two-year study consisted of thrombosis and degeneration of the liver, fibrosis of the spleen, and lymphoid hyperplasia. Degeneration of the eye was observed in low dose female rats (~1,200 mg/kg/d). This later effect has been correlated with exposure to artificial light due to cage placement, and as a result, long term studies presently incorporate cage rotation into the study design. The DBDPO two-year study was conducted prior to NTP instituting cage rotation as a part of their experimental protocols.

n mice, granulomas in the liver of low dose males and hypertrophy in the liver of low (~3,200 mg/kg/d) and high (~6,650 mg/kg/d) dose males were observed. Follicular cell hyperplasia was observed in thyroid glands of dosed male mice. The U.S. NTP concluded " ... effects observed in these studies must be attributed to the approximately 95% pure preparation used rather than to pure decabromodiphenyl oxide" (NTP 1986).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : oral feed
Exposure period : two years
Frequency of treatm. : continually in the diet
Post exposure period : no
Doses : 2.5 or 5% in the diet
Control group : yes, concurrent no treatment
Method : other
Year : 1986

GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : U.S. NTP Two Year Studies in Rats and Mice (1986)

Doses of 2.5 or 5% DBDPO in the diet for two years (103 weeks) were also well tolerated by F344/N rats (n=50 rats/sex/dose) and B6C3F1 mice (n=50 mice/sex/dose) with no effect on body weight or mortality and only minimal evidence of organ effects (NTP 1986). The U.S. National Toxicology Program (NTP) estimated the average amount of DBDPO consumed per day in the two year study to be 1,120 mg/kg and 2,240 mg/kg for low and high dose male rats, respectively, and 1,200 mg/kg and 2,550 mg/kg for low and high dose female rats, respectively. Likewise, NTP estimated the average DPDPO consumed per day by mice in the two year study was 3,200 and 6,650 mg/kg for low and high dose male mice, respectively, and 3,760 and 7,780 mg/kg for low and high dose female mice, respectively. The test article used in this study consisted of two lots of DBDPO that were 96% or 94-97% pure DBDPO, respectively.

Animals used in the 2-year study were produced under strict barrier conditions at Charles River Breeding Laboratories. Animals were shipped to the test laboratory at 5-6 weeks of age, quarantined for 14 (rats) or 16 (mice) days, and placed on the study when 7-8 (rats) and 9 (mice) weeks old. Animals were housed in polycarbonate cages with heat-treated hardwood chips. Rats and female mice were housed 5/cage, male mice 5/cage until month 8 and then 1/cage for intermittent periods, and 1/cage after 15 months. The animal room environment was 68-80 degrees F, 15-90% humidity, fluorescent lighting 12 hours/d, and with 10-12 room air changes/hour. Animals were randomized to groups by weight class and then to dose groups. Formulated or control diets and water were available ad libitum. The formulated diets were checked for homogeneity and correctness of concentration.

Animals were observed twice per day, weighed initially and then once/week for 12 weeks and monthly thereafter until wk 100 or 101 when observations were performed every 2 weeks. All animals were subjected to a necropsy and histologic examination of tissues. The tissues examined histologically were gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, sternum (including bone marrow), thymus, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, pancreas, gallbladder (mice), small intestine, colon, mesenteric lymph nodes, liver, spleen, kidneys, adrenal glands, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary gland, tissue masses, and regional lymph nodes. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Organ effects reported in high dose male rats (~2,240 mg/kg/d) at the conclusion of NTP's two-year study consisted of thrombosis and degeneration of the liver, fibrosis of the spleen, and lymphoid hyperplasia. Degeneration of the eye was observed in low dose female rats (~1,200 mg/kg/d). This later effect has been correlated with exposure to artificial light due to cage placement, and as a result, long term studies presently incorporate cage rotation into the study design. The DBDPO two-year study was conducted prior to NTP instituting cage rotation as a part of their experimental protocols.

In mice, granulomas in the liver of low dose males and hypertrophy in the liver of low (~3,200 mg/kg/d) and high (~6,650 mg/kg/d) dose males were observed. Follicular cell hyperplasia was observed in thyroid glands of dosed male mice. The U.S. NTP concluded " ... effects observed in these studies must be attributed to the approximately 95% pure preparation used

rather than to pure decabromodiphenyl oxide" (NTP 1986).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (127)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	30 days
Frequency of treatm.	:	continually in the diet
Post exposure period	:	no
Doses	:	0.01, 0.1 and 1.0% (~8, 80 and 800 mg/kg bw)
Control group	:	yes, concurrent no treatment
NOEL	:	= .01 %
Method	:	other
Year	:	1973
GLP	:	no data
Test substance	:	other TS: 77% DBDPO
Attached document	:	30-Day Repeated Dose Study (1973)

An earlier repeated dose study using a DBDPO material of lower (77%) purity, Dow FR-BA-300 (Norris et al. 1973, 1974, 1975), produced somewhat different results from those of NTP which used a test article of ~95% DBDPO (NTP 1986). This DBDPO mixture is no longer manufactured, and has not been manufactured since the mid-1980s.

In a 30-day feeding study 5 male Sprague-Dawley rats/group were administered the DBDPO mixture in the diet at 0, 0.01, 0.1 and 1.0%, which corresponded approximately 0, 8, 80 and 800 mg/kg body weight (Norris et al. 1973, 1974, 1975). No overt signs of toxicity were detected in any dose group. Liver weights were statistically increased in the 1.0 and 0.1 % dose groups compared to the control group. Gross pathologic changes were limited to hepatomegaly in 2 of 5 rats at the 1.0% dose level. Centrilobular cytoplasmic enlargement with minimal vacuolation was observed in 2 of 5 rats at the 1.0% dose level. Thyroid hyperplasia was detected in a non-dose-related manner: in 1 of 5 rats at the 1.0% dose level and in 3 of 5 rats at the 0.1% dose level. Hyaline droplet tubular cytoplasmic changes were detected in the kidneys of 4 of 5 rats at the 1.0% dose level. A dose of 8 mg/kg per day was established as a no-effect level and 80 mg/kg per day as a marginal-effect level. The 77% DBDPO commercial product is no longer manufactured and the results of the 1974 30-day study are not applicable to the >= 97% DBDPO commercial product in use today.

Reliability	:	(2) valid with restrictions

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5.5 GENETIC TOXICITY ‘IN VITRO‘

Type	:	Ames test
System of testing	:	S. typhimurium tester strains TA98, TA100, TA 1535 and TA 1637 and E. coli tester strain WP2 uvrA
Test concentration	:	15 to 5000 ug/plate
Cycotoxic concentr.	:	not cytotoxic
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1998

GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO (>98% purity) was tested in the bacterial reverse mutation assay using S. typhimurium tester strains TA98, TA100, TA 1535 and TA 1637 and E. coli tester strain WP2 uvrA in the presence and absence of Arochlor-induced rat liver S9 (Wagner and Klug 1998). The assay was performed in two phases, using the plate incorporation method. The first phase, the preliminary toxicity-mutation assay, was used to establish the dose range for the mutagenicity assay and to provide a preliminary mutagenicity evaluation. The second phase, the mutagenicity assay, was used to evaluate and confirm the mutagenic potential of the test material. Positive controls plated concurrently were 2-aminoantracene, 2-nitrofluorene, sodium azide, 9-aminoacridine, and methyl methanesulfonate. Dimethyl sulfoxide was selected as the solvent based on solubility of the test article and compatibility with the target cells. Concentrations from 50 to 250 mg/ml were workable suspensions. In the preliminary assay, the maximum dose tested was 5,000 ug/plate; this dose was achieved using a concentration of 100 mg/ml and a 50 uL plating aliquot. The test article was soluble but cloudy in dimethyl sulfoxide at < 3.0 mg/ml and soluble and clear at < 0.3 mg/ml. Precipitate was generally observed at > 500 ug/plate but no appreciable toxicity was observed. Based on the findings of the toxicity-mutation assay, the maximum dose plated in the mutagenicity assay was 5,000 ug/plate. In the mutagenicity assay, no positive response was observed. Precipitate was generally observed at >500 ug/plate but no appreciable toxicity was observed. Under the conditions of this study, DBDPO was concluded to be negative in the Bacterial Reverse Mutation Assay. This study was conducted according to US EPA and OECD guidelines and Good Laboratory Practices. Similar results were reported by the U.S. NTP in their own tests (NTP 1986).
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (127) (128)

Type	:	Mouse lymphoma assay
System of testing	:	L5178Y/TK+- mouse lymphoma cells
Test concentration	:	7, 8, 9, 10 ug/ml
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1986
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	DBDPO (the test article used in the NTP 2 carcinogenicity studies) was tested for muagenicity in L5178Y/TK+/- mouse lymphoma cells in the presence and absence of S9 (NTP 1986). Experiments were performed twice, and all doses were tested in duplicate, except the solvent control (DMSO), which was tested in triplicate. Cells (6 x 105/ml) were treated for 4 hours at 37 degrees C in medium, washed, resuspended in medium, and incubated for 48 hrs at 37 degrees C. After expression, 3 x 106 cells were plated in medium supplemented with trifluorothymidine for selection of cells

that were mutant at the thymidine kinase (TK) locus, and 600 cells were plated in nonselective medium to determine the percentage of viable cells.

DBDPO did not induce mutations in this mouse lymphoma assay.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Sister chromatid exchange assay
System of testing : Chinese Hamster Ovary cells
Test concentration : 50, 100, 250, 500 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1986
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : DBDPO (the test article used in the NTP 2 year carcinogenicity studies) was tested for the induction of sister-chromatid exchanges in Chinese hamster ovary cells in the presence or absence of S9 (NTP 1986). In the absence of S9, Chinese hamster ovary cells were incubated with DBDPO or solvent for 2 hr at 37 degrees C. BrdU was added, and incubation was continued for 24 hr. Cells were washed, fresh medium containing BrdU (10 uM) and colcemid (0.1 ug/ml) was added, and incubation was continued for 2-3 hrs. Cells were collected by mitotic shake-off, treated for 3 minutes with potassium chloride (75 mM), washed twice with fixative, dropped onto slides and air dried. Staining was by a modified technique (after Perry and Wolff, 1974; Goto el al.1978). In the presence of S9, cells were incubated with DBPDO or solvent for 2 hrs at 37 degrees C. Cells were washed, and medium containing 10 uM BrdU was added. Cells were incubated for a further 26 hrs, with colcemid (0.1 ug/ml) for the final 2-3 hrs. S9 was derived from the livers of Arochlor 1254-induced male Sprague-Dawley rats. DBDPO did not induce sister-chromatid exchanges in Chinese Hamster Ovary cells when tested with or without metabolic activation.

Reliability : (3) invalid
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Chromosomal aberration test
System of testing : Chinese Hamster Ovary cells
Test concentration : 50, 100, 250, 500 ug/ml
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1986
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : DBDPO (the test article used in the NTP 2-year carcinogenicity studies) was tested for induction of chromosome aberrations in Chinese hamster ovary cells with and without metabolic activation (NTP 1986). In the absence of S9, Chinese hamster ovary cells were incubated with DBDPO or solvent of 8-10 hrs at 37 degrees C. Cells were washed and fresh medium containing colcemid (0.1 ug/ml) was added. After a further 2-3 hr incubation, cells were harvested by mitotic shake-off, fixed, and stained with 6% Giemsa. In the presence of S9, cells were incubated with DBDPO or solvent for 2 hrs at 37 degrees C. Cells were washed, medium added and incubation continued for 8-10 hrs. Colcemid (0.1 ug/ml) was added for the last 2-3 hrs of incubation. Cells were harvested and fixed as described

for the sister-chromatid exchange test. S9 was derived from the livers of Arochlor 1254-induced male Sprague-Dawley rats.

DBDPO did not induce chromosome aberrations in Chinese hamster ovary cells when tested with or without metabolic activation.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (127)

Type : Ames test
System of testing : Salmonella typhimurium
Test concentration : 100, 333, 1000, 3333, 10,000 ug/plate
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1986
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (10)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Cytogenetic assay
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 60 days prior to mating, and subsequently throughout mating, gestation and lactation
Doses : 3, 30 or 100 mg/kg/d
Result : negative
Method : other
Year : 1975
GLP : no data
Test substance : other TS:77% DBDPO

Attached document : No cytogenic changes were observed in the bone marrow of rats (parents and offspring) undergoing a one-generation reproduction test using a former DBDPO-commercial mixture of 77% purity (Dow FR-BA-300) (Norris et al. 1975). This one-generation study was described in the section 5.8.3.
Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
01.08.2005 (121)

5.7 CARCINOGENICITY

Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : two years
Frequency of treatm. : continually in the diet
Post exposure period : no
Doses : 2.5 or 5% of the diet

Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : U.S. NTP Two Year Studies in Rats and Mice (1986)

Three groups of F344/N rats (n=50 rats/sex/dose) and B6C3F1 mice (n=50 mice/sex/dose) were fed diets containing 0, 2.5% or 5% DBDPO for 2 years (see Section 5.4 for a description of the study's conduct). The test article consisted of two lots of DBDPO that were of 96% and 94-97% pure, respectively. Doses up to 5% of the diet for two years were well tolerated by F344/N rats and B6C3F1 mice with no effect on body weight or mortality and only minimal evidence of organ effects (NTP 1986). The U.S. National Toxicology Program (NTP) estimated the average amount of DBDPO consumed per day in the two year study was 1,120 mg/kg and 2,240 mg/kg for low and high dose male rats, respectively, and 1,200 mg/kg and 2,550 mg/kg for low and high dose female rats, respectively. Likewise, NTP estimated the average DPDPO consumed per day by mice in the two year study was 3,200 and 6,650 mg/kg for low and high dose male mice, respectively, and 3,760 and 7,780 mg/kg for low and high dose female mice, respectively.

No evidence of carcinogenicity was observed in female mice receiving 2.5 or 5% DBDPO in the diet (~3,760 or 7,780 mg/kg/d).

Equivocal evidence of carcinogenicity was observed in male mice by an increase in the combined incidence of hepatocellular adenomas or carcinomas in both dose groups (~3,200 or 6,650 mg/kg/d); however, this finding may have been influenced by the larger number of early deaths in control male mice compared to the treated male mice. The large number of early deaths in the control males may have decreased expression of hepatocellular adenomas or carcinomas in this group. The combined incidence of hepatocellular adenomas and carcinomas in male mice treated with DBDPO was well within the historical range.

Some evidence of carcinogenicity(1) in male and female rats was observed by increased incidences of neoplastic nodules of the liver in low dose (2.5%, ~1,120 mg/kg/d) males and high (5%, ~2,240 mg/kg/d - males, ~2,550 mg/kg/d - females) dose groups of each sex. (The term "neoplastic nodule" is no longer used by NTP to describe hepatoproliferative lesions in rats. This change in nomenclature was made subsequent to a peer review of representative hepatoproliferative lesions from two-year carcinogenicity studies. The peer review found the use of this poorly defined and understood term had permitted some potentially useful drugs and chemicals to be unfairly categorized as carcinogens (Maronpot et al., 1986). DBDPO is not listed as a carcinogen by NTP (NTP 2001), the International Agency for Research on Cancer (IARC 1990) or the U.S. Occupational Safety and Health Administration (OSHA 1990).

(1) Five categories are used by NTP to describe results of their carcinogenicity studies: clear evidence of carcinogenicity, some evidence of carcinogenicity, equivocal evidence of carcinogenicity, no evidence of carcinogenicity, and inadequate evidence of carcinogenicity. These 5 categories are clearly defined in the final report of the studies.

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (129) (130) (127) (131)

Species : mouse

Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	two years
Frequency of treatm.	:	continually in the diet
Post exposure period	:	no
Doses	:	2.5 or 5% of the diet
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : U.S. NTP Two Year Studies in Rats and Mice (1986)

Three groups of F344/N rats (n=50 rats/sex/dose) and B6C3F1 mice (n=50 mice/sex/dose) were fed diets containing 0, 2.5% or 5% DBDPO for 2 years (see Section 5.4 for a description of the study's conduct). The test article consisted of two lots of DBDPO that were of 96% and 94-97% pure, respectively. Doses up to 5% of the diet for two years were well tolerated by F344/N rats and B6C3F1 mice with no effect on body weight or mortality and only minimal evidence of organ effects (NTP 1986). The U.S. National Toxicology Program (NTP) estimated the average amount of DBDPO consumed per day in the two year study was 1,120 mg/kg and 2,240 mg/kg for low and high dose male rats, respectively, and 1,200 mg/kg and 2,550 mg/kg for low and high dose female rats, respectively. Likewise, NTP estimated the average DPDPO consumed per day by mice in the two year study was 3,200 and 6,650 mg/kg for low and high dose male mice, respectively, and 3,760 and 7,780 mg/kg for low and high dose female mice, respectively.

No evidence of carcinogenicity was observed in female mice receiving 2.5 or 5% DBDPO in the diet (~3,760 or 7,780 mg/kg/d).

Equivocal evidence of carcinogenicity was observed in male mice by an increase in the combined incidence of hepatocellular adenomas or carcinomas in both dose groups (~3,200 or 6,650 mg/kg/d); however, this finding may have been influenced by the larger number of early deaths in control male mice compared to the treated male mice. The large number of early deaths in the control males may have decreased expression of hepatocellular adenomas or carcinomas in this group. The combined incidence of hepatocellular adenomas and carcinomas in male mice treated with DBDPO was well within the historical range.

Some evidence of carcinogenicity(1) in male and female rats was observed by increased incidences of neoplastic nodules of the liver in low dose (2.5%, ~1,120 mg/kg/d) males and high (5%, ~2,240 mg/kg/d - males, ~2,550 mg/kg/d - females) dose groups of each sex. (The term "neoplastic nodule" is no longer used by NTP to describe hepatoproliferative lesions in rats. This change in nomenclature was made subsequent to a peer review of representative hepatoproliferative lesions from two-year carcinogenicity studies. The peer review found the use of this poorly defined and understood term had permitted some potentially useful drugs and chemicals to be unfairly categorized as carcinogens (Maronpot et al., 1986). DBDPO is not listed as a carcinogen by NTP (NTP 2001), the International Agency for Research on Cancer (IARC 1990) or the U.S. Occupational Safety and Health Administration (OSHA 1990).

(1) Five categories are used by NTP to describe results of their carcinogenicity studies: clear evidence of carcinogenicity, some evidence of carcinogenicity, equivocal evidence of carcinogenicity, no evidence of

carcinogenicity, and inadequate evidence of carcinogenicity. These 5 categories are clearly defined in the final report of the studies.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (129) (130) (127) (132)

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 100 to 105 weeks
Frequency of treatm. : continually in the diet
Post exposure period : no
Doses : 0.01, 0.1 or 1 mg/kg bw/d
Result : negative
Control group : yes, concurrent no treatment
Method : other
Year : 1975
GLP : no data
Test substance : other TS: 77% DBDPO

Attached document : Two Year Study in Rats using 77% DBDPO test article

Groups of 25 male and 25 female Sprague?Dawley rats were fed 0, 0.01, 0.1 or 1 mg/kg body weight/day of a DBDPO-mixture (Dow FR BA-300: DBDPO 77.4%, NBDPO 21.8%, OBDPO 0.8%) in the diet for 100 to 105 weeks. Ingestion of up to 1 mg/kg/day of the DBDPO mixture did not influence survival rates; appearance, mean body weights, feed consumption, hematology, urinalysis, clinical chemistry (blood urea nitrogen, alkaline phosphatase and glutamic pyruvic transaminase activities) and organ weights of treated groups were similar to those of controls. Gross and microscopic examinations performed on all rats killed or dying during the course of the study, did not reveal any significant finding, all the observed changes or variations from normal occurred with similar frequency and severity in the treated and control groups of rats. All these changes were considered spontaneous in nature and unrelated to ingestion of the test article. No significant difference in the number of rats developing tumours, the total number of tumours or the specific type of tumours was observed between treated and control groups (Kociba et al. 1975).

29.07.2005 (133)

5.8.1 TOXICITY TO FERTILITY

Type : One generation study
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 60 days prior to mating, and subsequently throughout mating, gestation and lactation
Frequency of treatm. : continually in the diet
Premating exposure period
Male : 60 d
Female : 60 d
Duration of test :
No. of generation studies :
Doses : 3, 30 or 100 mg/kg/d
Control group : yes, concurrent no treatment

NOAEL parental	:	> 100 ml/kg bw
Result	:	did not affect fertility
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	other TS: 77% DBDPO
Attached document	:	One Generation Study in the Rat (1975): 77% DBDPO See Section 5.8.3 for details.
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

04.08.2005 (37)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	gestation days 0-19
Frequency of treatm.	:	once daily
Duration of test	:	gestation days 0-19
Doses	:	100, 300 or 1000 mg/kg bw/d
Control group	:	yes, concurrent vehicle
other:NOEL Maternal	:	>= 1000 mg/kg bw
other: NOEL Terato	:	>= 1000 ml/kg bw
Result	:	negative for maternal or fetal toxicity; negative for teratogenicity
Method	:	EPA OPPTS 870.3700
Year	:	2000
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	Rat Developmental Study (2002): >= 97% DBDPO as test article No evidence of maternal or fetal toxicity or developmental effects was detected in a developmental test in the Sprague Dawley rat (CD [Crl:CD(SD)GS BR) (n = 25 pregnant females/dose) at 1,000 mg/kg body weight utilizing a composite of today's commercial DBDPO product produced by three manufacturers and administered from days 0 - 19 of gestation (Hardy et al. 2002; Schroeder 2000). The test article composition was 97.34% DBDPO, 2.66% nona- and octabromodiphenyl oxide congeners. This study was performed according to current EPA and GLP guidelines. In this study, female rats (25 mated females/group) received 0, 100, 300 or 1,000 mg DBPDO/kg/day via gavage in corn oil from Gestation Day 0-19. All dams survived until scheduled sacrifice. No clinical signs of toxicity were observed. Pregnancy rates in the control and treated groups ranged from 96-100% and provided 23 or more litters in each group for evaluation on Gestation Day 20. No effect of treatment was detected in maternal gestational parameters (body weight, body weight gain and food consumption), uterine implantation data, liver weight or necropsy findings. Likewise, no treatment-related effect was detected in fetal body weights, fetal sex distribution, or from the fetal external, visceral, or skeletal examinations. The NOEL (No Observable Effect Level) for maternal and developmental toxicity was 1,000 mg DBPDO/kg/day, the highest dose level tested.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

03.08.2005 (134) (135)

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	gestation days 6-15
Frequency of treatm.	:	continually in the diet
Duration of test	:	gestation days 6-15
Doses	:	10, 100, or 1,000 mg/kg/day
Control group	:	yes, concurrent no treatment
NOAEL teratogen.	:	= 1000 mg/kg bw
other:NOEL MaterTox	:	>= 1000 - mg/kg bw
Result	:	negative for maternal toxicity and developmental effects
Method	:	other
Year	:	1973
GLP	:	no data
Test substance	:	other TS: 77% DBDPO

Attached document : Rat Developmental Toxcity Study (1973): 77% DBDPO

An earlier developmental study, using the former commercial product of only 77% DBDPO purity (Dow FR-BA-300) and administered to female Sprague-Dawley rats (n=20/treatment group and 30/control) on gestation days 6-15 at doses of 0, 10, 100, or 1,000 mg/kg/day, also was negative for maternal toxicity and developmental effects (Norris et al. 1973; 1974; 1975). The test article used by Norris et al., FR-300 BA, was a product composed of 77.4% DBPDO, 21.8% NBDPO, and 0.8% OBDPO, and is no longer manufactured.

No maternal toxicity or mortality was observed, and the mean maternal liver weights of the treated groups were statistically comparable to the control mean. No statistical differences between the control and treated groups were observed for the position and number of fetuses in utero, number of corpora lutea/dam, individual pup weight, crown rump ratio, sex ratio, number of litters, implantation sites/litter, live fetuses/litter, litters totally resorbed, or resorptions/litters with resorptions. The numbers of resorptions/implantation sites and the number of litters with resorptions was statistically significantly increased in the treated groups compared to control.

The statistical increase in resorption rate was secondary to an unusually low control value, showed no dose-response relationship, and was comparable to historical control values. Soft tissue variations detected in higher incidence in the 1,000 mg/kg dose group, but not in the 100 or 10 mg/kg groups, compared to control group were subcutaneous edema and delayed ossification of the interparietal bones of the skull.

Reliability : (2) valid with restrictions
03.08.2005 (31) (83) (121)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other: one generation reproduction
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	60 days prior to mating, and subsequently throughout mating, gestation and lactation

Frequency of treatm.	:	continually in the diet
Duration of test	:	60 days prior to mating, and subsequently throughout mating, gestation and lactation
Doses	:	3, 30 or 100 mg/kg/d
Control group	:	yes, concurrent no treatment
Result	:	no effect on reproduction
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	other TS: 77% DBDPO

Attached document : One Generation Study in the Rat

No adverse effects in either parent or F1 offspring were noted in a dietary one-generation reproduction test in male and female Sprague-Dawley rats utilizing doses up to and including 100 mg of a 77% DBDPO mixture (FR-300 BA)/kg body weight (Norris et al. 1975). The test article was composed of 77.4% DBDPO, 21.8% nonabromodiphenyl oxide, and 0.8% octabrmodiphenyl oxide. This DBDPO mixture is no longer manufactured, and has not been manufactured since the mid-1980s.

Groups of male and female rats were maintained on diets containing sufficient test article to provide dose levels of 0, 3, 30 or 100 mg/kg/d for 60 days prior to mating, during mating, and subsequently throughout gestation and lactation. There were 10 males and 20 females at the 2 lower dose levels, and 15 and 30 males and females, respectively at the high dose level. Twenty male and 40 female rats served as controls. The additional males and females were included with the controls and the group receiving the high dose level for tissue analysis for content of DBDPO. After 60 days on the test diet, each male was placed with 2 female from the same treatment regimen for 15 days (3 estrus cycles). After the 15-day mating period, the males and females were separated and maintained on the appropriate treatment diets. The females continued to receive the test diets throughout gestation and for 21 days following parturition. After 21 days of lactation, the females and their young were killed and necropsied. The brain, heart, liver, kidneys, and testes of 10 adult males and females in each group were removed and weighed. Microscopic examination of approximately 30 tissues was performed on 5 animals/sex in the control and high dose groups. Serum chemistries (BUN, alkaline phosphatase, and serum glutamic pyruvic transaminase) and urinalysis were performed on the control and high dose animals at termination (~ day 120). Sections of brain, liver, kidney, pancreas, spleen, heart, lung, testes/ovaries, adrenal gland, small intestine, large intestine, urinary bladder, and uterus were preserved from one male and one female of each litter for microscopic examination. After gross exam, the remaining weanlings of each litter were prepared for skeletal exam. Bone marrow was saved from 5 male and 5 female adults and weanling animals/dose level at termination of the study for cytogenic evaluation. Statistical evaluation of the indices of reproduction was made by the Fisher exact probability test. Analysis of the neonatal and maternal body weights and organs weights were made by an analysis of variance and the means were compared to control values by Dunnett's test. The level of significance chosen for all was $P<0.05$.

The results of this study indicate that incorporation of the DBDPO mixture in the diet of rats for 60 days prior to mating, and subsequently throughout mating, gestation and lactation had no effect on reproductive parameters. No signs of toxicity were observed in the adult rats or the neonates during the study or at necropsy. Unaffected parameters included body weight gain and food consumption by adults, reproductive parameters (the percent pregnant and neonatal growth, survival and development), pre-terminal urinalyses and clinical chemistry measures in adult rats, gross examination of all adult and weanling animals and microscopic examination of selected

tissues from both age groups. Cytogenic aberrations were not detected in bone marrow collected from the femurs of adults or weanlings. Thus, no toxicological manifestations were associated with ingestion of the DBDPO mixture at the highest dose level tested, 100 mg/kg/d.

Reliability : (2) valid with restrictions
Flag : Risk Assessment, Critical study for SIDS endpoint
03.08.2005 (121)

5.9 SPECIFIC INVESTIGATIONS

Endpoint : Immunotoxicity
Study descr. in chapter :
Reference :
Type :
Species :
Sex :
Strain :
Route of admin. :
No. of animals :

Attached document : DBDPO has not been evaluated for immunotoxicity using the OPTS 870.7800 guideline that is intended to provide information on suppression of the immune system that might occur as a result of repeated exposure to a test chemical. However, data available from long-term studies conducted in two species at high doses indicate DBDPO is not immunotoxic. DBDPO at 2.5 and 5% of the diet and administered for two years to rats and mice did not affect mortality or body weight (NTP 1986). If DBDPO was toxic to the immune system, deaths, decreased body weights and histologic evidence of infections would be expected. This was not the case. Routine histopathology of organs/tissues of the immune system also provide no evidence of toxicity. Organs of the immune system examined histologically in the NTP studies were the mandibular lymph nodes, sternum including bone marrow, mesenteric lymph nodes, spleen, and regional lymph nodes. Complete blood counts in the 30-D and 2-year studies (Norris et al. 1973, 1974; Kociba et al. 1975) were considered normal, and no histologic evidence of immunotoxicity was observed in the mesenteric and thoracic lymph nodes or sternal bone marrow. DBDPO's poor bioavailability reinforces a low potential for an adverse effect on the immune system.
15.08.2005 (133) (31) (36) (10)

Endpoint : Neurotoxicity
Study descr. in chapter :
Reference :
Type :
Species :
Sex :
Strain :
Route of admin. :
No. of animals :

Attached document : The neurotoxicity screening battery (OPPTS 870.6200) consists of a functional observational battery, motor activity, and neuropathology. The functional observational battery consists of noninvasive procedures designed to detect gross functional deficits in animals and to better quantify behavioral or neurological effects detected in other studies. The motor activity test uses an automated device that measures the level of activity of an individual animal. The neuropathological techniques are designed to provide data to detect and characterize histopathological changes in the central and peripheral nervous system. This battery is designed for use in conjunction with general toxicity studies and changes should be evaluated

in the context of both the concordance between functional neurological and neuropatholgical effects, and with respect to any other toxicological effects seen. This test battery is not intended to provide a complete evaluation of neurotoxicity, and additional functional and morphological evaluation may be necessary to assess completely the neurotoxic potential of a chemical.

DBDPO has not been specifically tested according to OPPTS 870.6200. However, no indication of neurotoxicity was observed in the NTP lifetime studies in rats and mice at exceptionally high doses (2.5 and 5% of the diet for two years) or in any of the other tests performed on DBDPO. These studies all included frequent observations for clinical signs of toxicity or effects on behavior that are essential components of the functional observational battery. Histopathology of the nervous system was normal in all studies.

Considering the high doses administered in the NTP 14-D, 13-Wk and 2-Yr studies to two species, ample opportunity was provided for induction and/or development of neurotoxicity. The fact that no evidence was detected indicates DBDPO is not neurotoxic. DBDPO's poor bioavailability reinforces a low potential for an adverse effect on the nervous system.

15.08.2005 (10)

Endpoint : other: Developmental Neurotoxicity
Study descr. in chapter :
Reference :
Type :
Species :
Sex :
Strain :
Route of admin. :
No. of animals :

Attached document : The developmental neurotoxicity study (OPPTS 870.6300) is designed to develop data on the potential functional and morphological hazards to the nervous system that may arise in the offspring from exposure of the mother during pregnancy and lactation. The test substance is administered to several groups of pregnant animals during gestation and early lactation, one dose level being used per group. Offspring are randomly selected from within litters for neurotoxicity evaluation. The evaluation includes observations to detect gross neurologic and behavioral abnormalities, determination of motor activity, response to auditory startle, assessment of learning, neuropathological evaluation, and brain weights. This protocol may be used as a separate study, as a follow-up to a standard developmental toxicity and/or adult neurotoxicity study, or as part of a two-generation reproduction study, with assessment of the offspring conducted on the second (F2) generation. Testing should be performed in the rat. Because of its differences in timing of developmental events compared to strains that are more commonly tested in other developmental and reproductive toxicity studies, it is preferred that the Fischer 344 strain not be used. If a sponsor wishes to use the Fischer 344 rat or a mammalian species other than the rat, ample justification reasoning for this selection must be provided.

While DBDPO has not undergone testing via OPPTS 870.6300, none of the repeated dose toxicology studies, including those administering DBDPO over the animals' lifetime, indicate an impact on the nervous system or on the developing embryo/fetus. The NOEL of DBDPO in a rat developmental toxicity study was 1,000 mg/kg/d administered on gestation days 0-19 (Hardy et al. 2002).

A non-guideline developmental neurotoxicity study of DBDPO in the mouse was briefly reported in 2001 (Viberg et al. 2001), and subsequently

published as a full paper (Viberg et al. 2003). DBDPO was reported to disrupt habituation in adult mice that were exposed via gavage on postnatal day (PND) 3, but not on PND 10 or 19, to a single oral dose of 20.1 mg DBDPO/kg. Animals exposed on neonatal day 3 to 2.3 mg/kg were not similarly affected nor were animals treated with either dose on neonatal day 19 or on neonatal day 10 with 1.34, 13.4 or 20.1 mg/kg. Detectable levels of radioactivity were reported in brain, heart and liver in animals at PND 3, 10 or 19.

No data was reported in the 4-page abstract, and much of the details relating to the study's performance and its results were not reported in the full publication. The composition of the test articles (PBDE 209 and 14C-PBDE 209) and their source was not specified. The test article/vehicle formulation was generated by dissolving the test article in a mixture of egg lecithin and peanut oil, and then using prolonged sonication with water to yield a 20% fat emulsion. The number of litters used to generate each treatment group ranged from 3-5, such that each treatment group contained more than one pup from each litter. Statistical analysis was based on individual pups, rather than on the litter as is standard procedure. Using the pup rather than litter as the experimental unit for statistical purposes grossly inflates the potential for false positive results (REF).

The neonatal mouse study was performed using an experimental design developed by P. Eriksson (Uppsala University, Sweden), and reported by Proff. Eriksson's graduate student. The design is not that typically used to investigate developmental neurotoxicity (e.g. is not equivalent to OPPTS 870.6300), and appears to be used almost exclusively in that laboratory. The probability is very low that DBDPO would produce an adverse effect in humans because of the very high dose administered in the Viberg et al. study, the lengthy exposure period required to cover a corresponding period in humans, DBDPO's poor oral absorption (less than 2% in the rat), rapid elimination (>99 % after 72 hours with a half-life less than 24 hours), poor solubility, and lack of bioaccumulation. These concepts are more fully developed below.

In several publications (Eriksson 1992; Eriksson and Talts, 2000; Eriksson 1997), Eriksson cites Davison and Dobbing (1968) as the source of information regarding the brain growth spurt, a key concept in the postnatal timing of dose administration in Eriksson's design. Davison and Dobbing (1968) state that the brain growth spurt occurs after birth in rats and mice, is almost complete at birth in guinea pigs, and occurs prior to birth in humans and primates: "The main fact which emerges is the very different timing of the brain growth spurt in relation to birth in different species, and it follows from this that such expression as 'foetal brain' or 'neo-natal' or 'post-natal brain' are quite meaningless unless one knows both the species being considered and the growth characteristics of its brain. Such an observation, which seems almost too obvious to mention, is very frequently ignored when interspecies extrapolations are being considered, especially when these are between man and other species." Eriksson and Talts (2000) state "The BGS does not take place at the same time point in all mammalian species. In the human, this period begins during the third trimester of pregnancy and continues throughout the first 2 years of life. In mouse and rat the BGS is neonatal, spanning the first 3-4 weeks of life."

Based on the timing of brain growth in humans, exposure would have occur during the last trimester of pregnancy and be followed by continued exposure during the first 2 years of the child's life in order to mimic exposure on neonatal mouse day 10. Assuming equal susceptibility in the child and mouse, absorption between 0.3-2% of an oral dose, and 100% transfer of the absorbed dose to the fetus, a 50 kg woman would have to receive a total dose of 50 to 1,000 mg DBDPO every day during the later stages of pregnancy followed by additional exposure to the child during the

first two years of its life to reach a dose equivalent to that administered to neonatal mice.

A similar calculation can be made with respect to mice. In terms of the dose a lactating mouse would have to receive in order to pass on an equivalent dose to her nursing offspring, neonatal day 3 is of interest with respect to Viberg's findings. On day 3 of life, the pup's total nutrition is received via nursing. Therefore, oral exposure to the pup at this age would be via milk. However, DBDPO's high molecular weight, its physical/chemical properties, and its pharmacokinetics, make it highly unlikely that DBDPO would be eliminated in the milk (see Section 5.3.7). Therefore, neonatal exposure via this route is not expected. Nonetheless, doses that a lactating mouse would have to receive in order to transmit in her milk doses equivalent to Viberg's are estimated below. The following conservative assumptions were used in calculating the dose received: Weight of the female mouse = 20 g, Weight of the day 3 neonate = 2.5 g based on an average birth weight of 1.5 g, 6 pups/litter (average litters range from 1-12 pups; Viberg did not provide the number pups/litter), Female mouse produces 10 % of her body weight/day in milk, 3% absorption of an oral DBDPO dose by the lactating mouse, 100% transfer of the dose to milk and 100% absorption of the dose by the pup.

Based on these assumptions,each pup would consume 0.33 g of milk, and the 2.2 and 20.1 mg/kg dose administered to the day 3 neonates would be equivalent to a total dose of 0.005 or 0.05 mg/pup, respectively. To achieve a total dose of 0.005 or 0.5 mg, the milk would have to contain 0.015 or 0.15 mg/g milk. The total day's milk production (2 g) would thus contain 0.03 or 0.3 mg total. Assuming the dam absorbed 3% of an oral dose,she would have to be exposed to doses of 50 or 500 mg/kg body weight in order to generate the estimated milk content. To achieve a dose of this amount, the dam would have to be exposed to 415.9 or 4,159 mg DBDPO/kg food.It is highly unlikely that lactating female mouse (or another mammalian species) could be exposed to a dose of 415.9 or 4,159 mg DBDPO/kg food except under laboratory conditions.

Using the results of the NTP mouse 2-year study, a dose of 25,000 ppm food, and assessment factor of 100, the oral predicted no effect concentration for a lifetime exposure would be 250 mg/kg food. The food exposure to a female mouse, 415.9 or 4,159 mg DBDPO/kg food, in order to generate doses in a day 3 neonate equivalent to those administered by Viberg (2001), are higher than the oral predicted no effect concentration calculated from the NTP two year mouse study.

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Endpoint : Endocrine System Modulation
Study descr. in chapter :
Reference :
Type :
Species :
Sex :
Strain :
Route of admin. :
No. of animals :

Attached document : DBDPO (administered as DE-83R) did not affect serum total thyroxin (T4), triiodothyroinine (T3) or thyroid-stimulating hormone (TSH) when administered to weanling rats at oral doses of 0.3, 1, 3, 10, 30, 60 or 100 mg/kg/d for 4 days (Zhou et al. 2001).

29.07.2005 (142)

Endpoint : other: hepatic enzyme induction

Study descr. in chapter :
Reference :
Type :
Species :
Sex :
Strain :
Route of admin. :
No. of animals :

Attached document : Gavage administration of DBDPO (0.1 nmol/kg/day) to rats over 14 days did not induce hepatic cytochrome P450, cytochrome P450 reductase, UDP-glucuronyl-transferase, benzo[a]pyrene hydroxylase, p-nitroanisole demethylase, or EPN detoxification (Carlson 1980).

Hepatic enzyme induction was not observed in weanling rats treated with DBDPO (oral, 0.3, 1, 3, 10, 30, 60 or 100 mg/kg/d) for 4 days. Hepatic enzyme activities measured were ethoxy- and pentoxy-resorufin-O-deethylase (EROD, PROD) and uridinediphosphate-glucuronosyltransferase (UDPGT) (Zhou et al. 2001).

01.08.2005 (143) (142)

5.10 EXPOSURE EXPERIENCE

Type of experience : Human

Attached document : Occupational Exposure

The American Industrial Hygiene Association (AIHA) established a Workplace Environmental Exposure Level (WEEL) for DBDPO of 5 mg/m3 based on DBDPO's toxicology data (AIHA 1996). A WEEL is the level at which at workers could be exposed every day for an 8-hour shift with the expectation of no adverse effects. The U.S. Occupational Safety and Health Agency (OSHA) has not set a Permissible Exposure Limit (PEL) for DBDPO. However, OSHA has set a PEL of 5 mg/m3 for the "respirable fraction of particulates not otherwise regulated", e.g. nuisance dusts. Thus, the AIHA WEEL for DBDPO is equivalent to that of a nuisance dust.

Workplace exposures to DBDPO may occur at a) manufacturing, and b) formulation into the resin or liquid polymer dispersion. DBDPO is manufactured in a closed system by the reaction of bromine with diphenyl oxide. The point at which exposure could occur during manufacture is when DBDPO is transferred into bags for shipping. Likewise, the point at which worker exposure is most likely during formulation is when the bags of flame retardant are emptied into a hopper prior to mixing. Once formulated, DBDPO is encased in the polymer matrix and the potential for worker exposure is negligible.

Theoretically, workplace exposure could occur via the dermal or inhalation routes. DBDPO's physical and chemical properties make the probability of systemic absorption following dermal or inhalation exposure very low. DBDPO is a large molecule of high molecular weight (959.17) with negligible water solubility (<0.1 ug/L), and is likely to diffuse through biological membranes only with great difficulty. This assumption is borne out with pharmacokinetic studies that demonstrate DBDPO's poor bioavailability. DBDPO's vapor pressure (4.63 x 10-6 Pa) is such that volatilization is not expected to be a source of inhalation exposure. Occupational exposure to dusts may occur, and the particle size of the DBDPO commercial product is within the inhalable and/or respirable range. The particle size used resin application is ~5 microns, whereas that used in textile applications is finely ground to ease its dispersion in latex coatings.

Any DBDPO particles present in air are likely to be associated with larger dust particles due to DBDPO's affinity for adsorption (estimated Koc = 1.796 x 106) (Meyland and Howard 1999). It is likely that the primary routes of absorption in the workplace are via incidental ingestion resulting from inhalation (and mucociliary escalator effect) and contaminated clothing and surfaces.

Theoretically, the flame retardant textile backcoat could crumble during fabrication of upholstered furniture. Any particles generated would likely be too large to be respirable. In addition, for systemic absorption to occur, not only would the particles need to be inhaled or ingested, but also DBDPO would have to diffuse out of the polymer prior to its absorption. Systemic absorption of significant amounts as a result of crumbling of the backcoat is highly unlikely.

An additional occupational exposure scenario explored in the published literature is electronics recycling, computer repair and rubber manufacture. DBDPO, and other polybrominated diphenyl oxide (a.k.a. ether) isomers, was detected in Swedish workers engaged in dismantling electronic equipment (Sjodin et al. 1999; Sjodin 2000) and in Swedish computer technicians (Hagmar et al. 2000). This work was performed as a Ph.D. research project (Sjodin 2000). These findings are discussed and the measured workplace air levels (0.0002 mg/m3) are compared to the AIHA WEEL for DBDPO of 5 mg/m3. Thuresson et al. (2002a,b) also reported detection of DBDPO in Swedish workers engage in rubber manufacturing and electronic shredding operations. Occupational blood and air levels are summarized.

Table 5-1. Measured DBDPO human serum and air concentrations in various occupations.

Type of Work	DBDPO Serum Levels(pmol/g lipid) Median	Number of Individuals	DBDPO Air Concentration	Reference
U.S.				
Manufacture	N.D.*	39 (all male)	0.21-5.9 mg/m3	Bahn et al. 1980; Bialik 1982
Sweden				
Electronics Recycling	5	19 (15 males, 4 females)	36 ng/m3	Sjodin et al. 1999; Sjodin 2000
Computer Repair	2	19 (15 males, 4 females)	N.R.+	Hagmar et al. 2000
Rubber Manufacture	32	19 (all male)	7.6 + 5.6 pmol/m3	Thuresson et al. 2002b
Electronics Shredding	3	5 **	13 pmol/m3	Thuresson et al. 2002a
Referents				
Hospital Cleaning	<0.7	20 (all female)	N.R.	Sjodin et al. 1999; Sodin 2000
Computer Clerks	<0.7	20 (all female)	N.R.	Sjodin et al. 1999; Sodin 2000
Abattoir Workers	3	18 (all male)	N.R.	Thuresson et al. 2002a,b

*N.D. = Not Detected (ng/ml serum)
**Gender distribution not provided.
+N.R. = Not Reported

AIHA established a WEEL of 5 mg/m3 for DBDPO. This WEEL is essentially that of a nuisance dust. Occupational exposure to dusts containing DBDPO may occur at the manufacturing site during bagging operations or when the bags are emptied into hoppers at the processing site. The particle size used resin applications is ~5 microns, whereas that

used in textile applications is finely ground to ease its dispersion in latex coatings. Any DBDPO particles present in air are likely to be associated with larger dust particles due to adsorption (estimated Koc = 1.796 x 106). DBDPO is a large molecule of high molecular weight (959.17) with negligible water solubility (<0.1 ug/L), and is likely to diffuse through biological membranes only with great difficulty based on oral pharmacokinetic studies. This, coupled with DBDPO's high no-adverse-effect level of 1,000 mg/kg/d in chronic studies, indicates the worker is not at risk of adverse effects due to dust exposure.

DBDPO oral absorption is minimal (<0.3 to 2% of an oral dose), but no data on its pulmonary absorption is available. Although the absorptive processes in the lung and gastrointestinal (GI) tract are similar, DBDPO absorption from the respiratory tract is expected to be less than from the GI tract. The respiratory membrane has a surface area of 160 m2 versus 250 m2 for the intestinal mucosal villi (Ritschel 1982), and the lung's absorptive surface is therefore ~64% of that of the small intestine. DBDPO has negligible solubility, and thus inhaled particle-bound DBDPO can be expected to behave similar to other inert insoluble particles deposited in the respiratory tract. Insoluble particles deposited within the ciliated airways of the respiratory tract (e.g., the nasal passages and tracheobronchial tree) undergo passive transport via the mucuciliary escalator to the pharynx and are subsequently swallowed (Lippman 1980). Insoluble particles reaching the alveoli are predominantly cleared by alveolar macrophages that phagocytize the particles and transport them proximally on the bronchial tree to be swallowed. Absorption of insoluble particles from the alveoli directly into the bloodstream is low and exceedingly slow. Thus, it appears unlikely that absorption of DBDPO from the respiratory tract is greater than that of the gastrointestinal tract.

Recent publications report detection of DBDPO in the blood of Swedish workers engaged in electronics recycling or computer repair (Sjodin et al. 1999; Sjodin 2000; Hagmar et al. 2000; Thuresson et al. 2002a) and in rubber manufacturing (Thuresson et al. 2002b). The studies in electronic recycling workers are the best documented of these papers and is discussed further in the following paragraphs.

The mean DBDPO blood levels reported were 5 pmol/g lipid in the Swedish electronics recycling workers, and 1.6 pmol/g lipid in the Swedish computer technicians. DBDPO air levels in the recycling workplace were 0.0002 mg/m3. The PCB 153 blood levels measured in the same workers was 760 pmol/g lipid in the dismantlers and 290 pmol/g lipid in the technicians. Greater than or equal to 99% of the DBDPO detected in air at the electronics dismantling plant was associated with particulate matter (Sjodin 2000).

The amount of a substance absorbed (Adose) through the respiratory tract over a given period of exposure can be calculated (Patty 1994) using the concentration in air in mg/m3 (Ac), the duration of exposure in hours (T), the ventilation rate in m3/hour (V), and the absorption rate (Abs):

Adose = AcTVAbs.

A theoretical DBDPO blood concentration can be calculated using the percent oral absorption as an indicator of respiratory uptake and the equation above. Using a maximum absorption of 2% of the dose, a ventilation rate of 10 m3/8 hr work shift and an exposure equivalent to the AIHA WEEL (5 mg/m3), the amount of DBDPO absorbed would be 1 mg/70 kg man or 0.014 mg/kg body weight. This is orders of magnitude less than DBDPO's reference dose (RfD) of 4 mg/kg-d calculated by NAS (2000). In the event that DBDPO's absorption was equal to 100%, the absorbed dose would still remain less than NAS's RfD. At 100% absorption and an exposure concentration of 5 mg/m3, the internal dose

would be 0.71 mg/kg body weight.

Using the equation Adose = AcTVAbs, a maximum absorption of 2% of the dose, a ventilation rate of 10 m3/8 hr work shift and at maximum measured DBDPO air concentration of 0.2 ug/m3 in the electronics dismantling plant (Sjodin et al. 1999), the absorbed dose would be 0.04 ug DBDPO/70 kg man or 0.57 ng DBDPO/kg body weight.

At a measured DBDPO serum lipid level of 4.8 ng/g lipid in the electronics dismantling workers (Sjodin et al. 1999), the DBDPO plasma level would be 0.0288 ng/ml plasma. Assuming 3,000 ml plasma in a 70 kg man and a normal plasma lipid concentration of 0.6% (Guyton 1986), the 0.0288 ng DBDPO/ml plasma represents a total blood volume content of 86.4 ng DBDPO/70 kg man or 1.2 ng/kg body weight. Thus, the theoretical DBDPO internal dose (0.57 ng/kg body weight) due to a measured air concentration of 0.2 ug/m3 compares favorably with the actual dose of 1.2 ng/kg body weight in the electronics dismantling workers calculated from their measured blood values. The theoretical and measured values are well within the variation expected due to the assumptions used in calculating the expected values and the collection and analytical methods.

The measured DBDPO air level at the electronic recycling plant was 0.0002 mg/m (Sjodin et al. 1999). The American Industrial Hygiene Association (AIHA) evaluated DBDPO's toxicology and set a Workplace Environmental Exposure Level (WEEL) of 5 mg/m3, e.g. that of a nuisance dust (AIHA 1996). Thus, the measured DBDPO air level at the electronics dismantling plant was 25,000 times below the AIHA level to which workers could be exposed every day with the expectation of no adverse effects. Further, using the equation Adose = AcTVAbs and a maximum absorption of 2%, the estimated internal DBDPO dose from an 8-hr exposure at the AIHA WEEL of 5 mg/m3 would be 0.014 mg/kg body weight. The internal dose of the electronic recycling workers was 1.2 ng/kg or 0.01% of the internal dose that could be received at a DBDPO exposure equal to the AIHA WEEL. Finally, in the event that DBDPO absorption from the respiratory tract was greater than 2%, the internal dose of the electronic recycling workers at a measured DBDPO air level of 0.0002 mg/m3 would remain substantially below that achievable at the AIHA WEEL. For example, if DBDPO absorption equaled 100%, the internal dose due to a workplace air level of 0.0002 mg/m3 would be 0.004% of that dose which could be received at a DBDPO exposure equal to the AIHA WEEL.

The DBDPO blood levels reported in Swedish electronics dismantling workers (5 pmol/g lipid) and computer technicians (1.6 pmol/g lipid) were extremely small and are representative of our increasing ability to detect minute amounts of chemicals in various media. Further, these values should be viewed as tentative given the difficulty of DBDPO analysis, the extremely low levels reported, and the problem of laboratory contamination contributing to measured values. The DBDPO blood levels were far below those of PCB 153 (dismantlers, 760 pmol/g lipid; technicians, 290 pmol/g lipid) measured in the same workers. The electronics dismantling workers' internal DBDPO dose (1.2 ng/kg body weight) based on their measured blood level was comparable to the level expected (0.57 ng/kg body weight) calculated from the measured air levels. A similar comparison was not possible for the computer technicians because air values were not reported for that workplace. In addition, the DBDPO measured air level (0.2 ug/m3) in the electronics recycling plant was approximately 25,000 times below the acceptable DBDPO workplace exposure level of 5 mg/m3. This acceptable workplace exposure level, set by the AIHA, was based on an evaluation of DBDPO toxicology data. Thus, no impact on human health from DBDPO is expected in either the electronics dismantlers or computer technicians.

Occupational Exposure Conclusions

DBDPO is used to flame retard synthetic polymers used in electrical and electronic equipment and upholstery. Once encapsulated in a polymer matrix, DBDPO will be essentially unavailable. Therefore, reasonable exposure routes/scenarios are as follows: a) inhalation of dust and/or dermal contact at manufacture and b) at formulation prior to encapsulation in polymer or inclusion in the textile dispersion.

The most likely point at which exposure could occur during manufacture is when the flame retardant is transferred into bags for shipping. Likewise, the point at which worker exposure is most likely during formulation into the polymer dispersion is when the bags of DBDPO are emptied into a hopper prior to mixing the dispersion. Once formulated into the polymer dispersion, DBDPO is encased in the polymer matrix and the potential for worker exposure is negligible.

Theoretically, workplace exposure could occur via the dermal or inhalation routes. DBDPO's low vapor pressure makes vapor inhalation an unrealistic exposure scenario. DBDPO's potential for dermal absorption is low based on its physical and chemical properties and the known requirements for absorption of any compound through the skin. DBDPO's very low water solubility and very high molecular weight effectively precludes any significant skin absorption, and DBDPO's skin absorption is estimated at <<0.03% of a dermally applied dose. Occupational exposures to dusts may occur; however, DBDPO is a very large poorly absorbed molecule that exhibits little toxicity, and for which AIHA has assigned a WEEL of 5 mg/kg/d. The combined effects of poor absorption and minimal toxicity (NOAEL m 1,000 mg/kg/d) indicate adverse effects should not occur as a results of occupational exposure. Nonetheless, workplace controls should focus on points where fine-particle-size-DBDPO may become airborne to limit inhalation exposure. This would be during bagging at manufacture and at formulation prior to inclusion in the resin or polymer dispersion.

08.08.2005 (12) (144) (145) (7) (146) (147) (148) (149)

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

Attached document : DBDPO's physical/chemical properties of very low solubility in both water and organic solvents, very low vapor pressure, and tendency to adsorb to surfaces make the substance an analytical challenge. DBDPO is difficult to vaporize when using the gas chromatograph, and has a very long retention time on columns commonly used for analysis of environmental samples. Laboratory and glassware contamination are significant issues that must be controlled and eliminated in order to achieve valid results when evaluating trace levels. Becuase of these challenges, reports of detection in various matrixes should be interpreted with caution. Careful attention should be paid to blanks and quality control.

Reliability : (1) valid without restriction

15.08.2005 (150) (151)

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

Memo : Conclusions from the DBDPO VCCEP Submission: Risk Assessment in Children

Attached document : Page 106-108 of the DBDPO VCCEP Submission:

DBDPO is used solely as a flame retardant, and in all applications is encapsulated in a polymer matrix with no direct consumer exposure. Its primary application is in electrical and electronic equipment with a secondary application in upholstery textiles. A typical U.S. application for DBDPO is in television cabinets composed of high impact polystyrene. DBDPO is not sold directly to the public.

DBDPO is a data rich chemical with virtually all VCCEP Tier I, II and III hazard endpoints fulfilled. It is a large poorly absorbed molecule that exhibits little toxicity. Testing has shown that DBDPO is not acutely toxic or mutagenic, and is not a developmental or reproductive toxicant. The NOAEL for DBDPO in subchronic and/or chronic studies in the rat or mouse is at least 1,000 mg/kg/d. DBDPO's low toxicity is likely related to its poor absorption and rapid elimination (NTP 1986). Pharmacokinetic studies have shown that DBDPO is poorly absorbed (0.3 -2% of an oral dose), has a short half-life (24 hr in rats) compared to PCB 153 (<2% of an oral dose was eliminated by rats in 21 days), and is rapidly eliminated in the feces (>99% in 72 hr in rats) (NTP 1986; Norris et al. 1973, 1975; El Dareer et al. 1987; Moreck and Klassen-Wheler 2001).

These features coupled with DBDPO's low potential for migration out of plastic resin are indicative of low risk. The U.S. National Academy of Sciences (NAS) evaluated the potential risk to the consumer posed by DBDPO-treated upholstery textiles. In all scenarios evaluated by NAS, dermal, oral or inhalation exposure to DBDPO was determined not to present a risk of adverse health effects to the consumer, including children mouthing upholstery textiles. A similar conclusion was reached in the current assessment with respect to exposures resulting from DBDPO's use in electrical and electronic applications. The WHO and the European Union also concluded the general population is at negligible risk from DBDPO.

Exposure to DBDPO could potentially occur through food or breast milk. However, DBDPO has not been detected in limited sampling of fish and poultry in the U.S., and based on its properties, is not anticipated to be present in these food items or in meat or dairy products. Likewise, leafy vegetables and root crops are not expected to be a source of DBDPO exposure to the general public, and a risk of adverse health effects is not anticipated.

DBDPO transfer to breast milk is likely to be slow and very limited, if at all. Protein binding, ion trapping and lipid partitioning are not expected to alter DBDPO concentrations in breast milk due to DBDPO's physical/chemical properties. Build-up of DBDPO concentrations in breast milk is not expected due to its anticipated slow diffusion into milk and periodic

emptying of breast milk. This combination of low absorption from the gut, rapid elimination in the feces, poor and/or slow diffusion into breast milk should effectively preclude DBDPO in milk. Thus, a risk to the nursing infant is not anticipated.

Highly conservative estimates of U.S. DBDPO pathway-specific and aggregate exposures (Table 6-1) are substantially lower than DBDPO's NOAEL of 1,000 mg/kg/d and the reference dose (RfD), 4 mg/kg/d, calculated by NAS (NAS 2000). These estimated exposures are intentionally biased to generate worst-case exposures; actual exposures in the U.S. are expected to be substantially lower. For noncancer health effects, quantitative risk estimates are typically provided in the form of Hazard Quotients (HQs). The HQ represents the estimated exposure for a specific chemical divided by the reference dose (RfD), expressed in mg/kg-day. As such, HQs indicate the calculated exposure estimates in comparison to an exposure level that is unlikely to result in adverse health effects. If an HQ value is less than one, then it can reasonably be assumed that the chemical exposure will not be associated with toxicity. As HQ values increase above one, the potential for toxicity increases. As shown in Table 6-1, all calculated HQs for DBDPO are significantly less than one, with the highest aggregate HQ of 0.2 being five-fold lower than one. Thus, these HQs indicate that even when using conservative, worst-case estimates of exposure to DBDPO, adverse health effects are not expected.

The protection provided by DBDPO in terms of enhanced fire safety reduces the very real risk of death or injury that consumers face in the home from fires. In the applications in which DBDPO is used, an estimated 280 lives are saved each year in the U.S. through the use of a brominated flame retardant. These estimated lives-saved are particularly relevant to the VCCEP program, because children are especially vulnerable to fire deaths and injuries. The benefits derived from the use of DBDPO in consumer products, particularly for children, far outweigh the insignificant potential for harm.

TABLE 6-1. DBDPO exposure estimates and hazard quotient based on a RfD of 4 mg/kg/day.

	Daily Intakes Estimate(mg/kg/d)		ExposureDuration(yrs) Hazard Quotient(RfD = 4 mg/kg/de)		Exposure	
	Reasonable Upper	Estimate	Upper	Reasonable	Estimate	
Pathway-specific						
Ingestion, breast milk-manufacturer	0-2	1.9E-02a	3.4E-01	0.005	0.09	
Ingestion, breast milk-disassembler	0-2	3.3E-06a	2.5E-05	8E-07	6E-06	
Ingestion, consumer electronics	0-2	4.3E-06	2.5E-04	1E-06	6E-05	
Ingestion, mouthing fabric (NAS)	0-2	2.6E-02	2.6E-02	0.007	0.007	
General exposures	0-70	1.2E-03	3.9E-01	0.0003	0.1	
Aggregate						
Infant, manufacturerb	--	0.046b	0.76b	0.01	0.2	
Infant, disassemblerc	--	0.027c	0.41c	0.007	0.1	
Lifetime (0-70)d	--	0.0012d		0.39d	0.0003	0.1

a Assumes a shorter duration for nursing (0-3 months), based on Collaborative Group on Hormonal Factors in Breast Cancer 2002.

b This value incorporates the intakes for ingestion of breast milk from a mother who is a manufacturer, plus ingestion from consumer electronic products, ingestion from mouthing fabric, and general exposures.
c This value incorporates the intakes for ingestion of breast milk from a mother who is a disassembler, plus ingestion from consumer electronic products, ingestion from mouthing fabric, and general exposures.
d This value incorporates the intake from general exposures. See text for details.
e The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data. The RfD for DBDPO, 4 mg/kg/d, was calculated by the U.S. National Academy of Sciences instead of using the current 1999 IRIS Rfd (0.01 mg/kg/d). NAS calculated a revised RfD for DBDPO using the NTP 2 year bioassay results, which were not available at the time of the IRIS derivation (1984-1985).

15.08.2005

Memo : Conclusions from the U.S. National Academy of Scienes: Risk to Consumers from Flame Retarded Upholstery

Attached document : NONCANCER ENDPOINTS

Dermal Exposure
NAS calculated a hazard index for dermal exposure for DBDPO using a dose rate of 1.33 x 10-9 mg/kg-d and the oral RfD of 4 mg/kg-d. The hazard index of 3.34 x 10-10, demonstrates DBDPO used as an upholstery fabric flame retardant is not likely ot pose a noncancer risk from dermal exposure.

Inhalation Exposure - Particulates
NAS developed a provisional RfC of 14 mg/m3. A hazard index of 3.4 x 10-5 was estimated based on an estimated exposure of 0.48 ug/m3. This indicates that under worst case exposure assumptions, DBDPO used as an upholstery fabric flame retardant does not pose any noncancer risk via inhalation of DBDPO in the particulate phase.

Inhalation Exposure - Vapors
Using the provisional RfC and an exposure of 3.8 x 10-4 mg/m3, NAS calculated a hazard index of 2.71 x 10-5 indicating that under the worst case scenario, exposure to DBDPO used as an upholstery fabric flame retardant is not likely to pose a noncancer risk via the inhalation route, when exposure occurs in the vapor phase.

Oral Exposure
Using an estimated dose of 2.6 x 10-2 mg/kg-d, NAS calculated a hazard index of 6.5 x 10-3, and concluded DBDPO used as an upholstery fabric flame retardant does not pose any noncancer risk via the oral route.

CANCER

Dermal Exposure
NAS calculated a lifetime risk estimate of 1.20 x 1012, and concluded this estimate is small enought that the cancer risk through dermal contact with DBDPO used as an upholstery fabric flame retardant can be considered negligible.

Inhalation Exposure
NAS calculated a cancer unit risk of 2.57 x 10-7 per ug/m3. From estimates of either particles or vapor, NAS concluded that the lifetime risk estimates

were 1.2 x 10-7 and 6.7 x10-7, respectively. NAS concluded these estimates indicate DBDPO used as an upholstery fabric flame retardant poses a negligible cancer risk via inhalation.

Oral Exposure
NAS calculated a lifetime average oral dose rate of 7.4 x 10-4 mg/kg-d, and a lifetime cancer risk estimate of 6.7 x 10-7. NAS concluded this estimate is small enough that he cancer risk via the oral route can be dismissed as negligible when DBDPO is used as an upholstery fabric flame retardant.

NAS 2000. Toxicological Risks of Selected Flame-Retardant Chemicals. National Academy Press. Washington, D.C. http://www.nap.edu.

15.08.2005

Memo : Conclusions from the EU Risk Assessment

Attached document : DBDPO was found to present no risk to human health or the environment after an exhaustive 10-year risk assessment that considered aquatic, mammalian, and terrestrial toxicology tests, and environmental and human monitoring.

15.08.2005

Memo : Conclusions from the WHO Environmental Health Criteria Document

Attached document : The WHO (1994) found DBDPO's use as a flame retardant did not present a risk to consumers.

15.08.2005

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8.2 *Environmental Science Technology*, "Levels of Polybrominated Diphenyl Ether (PBDE) Flame Retardants in Animals Representing Different Trophic Levels of the North Sea Food Web"

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